

# Toxicology Research Laboratory

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at Chicago

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20100915167

Title Page

Volume 2 of 2

**D**raft Report for Task Order No. UIC-7J

**F**OUR WEEK ORAL TOXICITY  
STUDY OF WR242511 IN DOGS

**A**Sponsor: US Army Medical Materiel  
Development Activity

**R**Test Article: WR242511

**C**Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

June 3, 1994

Performing Laboratory

TOXICOLOGY RESEARCH LABORATORY (TRL)  
University of Illinois at Chicago (UIC)  
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APPENDIX 5

Individual Food Consumption Data

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

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INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 1-M

SEX: MALE

DOSE: 0 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8172	185	194	245	338	330	360
8143	232	361	400	319	306	285
8148	160	400	266	360	279	202
8153	253	149	243	400	399	293

MEAN	208	276	289	354	329	285
S.D.	42.6	123.1	75.1	34.8	51.4	64.8
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 2-M

SEX: MALE

DOSE: 0.1 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8173	243	234	400	400	384	381
8170	256	349	185	262	400	224
8147	322	284	400	400	400	400
8151	184	283	289	400	400	275

MEAN	251	288	319	366	396	320
S.D.	56.6	47.2	103.2	69.0	8.0	84.4
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 3-M

SEX: MALE

DOSE: 0.3 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8157	127	400	400	400	400	400
8159	246	165	269	339	180	236
8175	226	400	400	367	400	400
8166	228	242	305	400	396	400

MEAN	207	302	344	377	344	359
S.D.	53.9	117.7	66.9	29.4	109.3	82.0
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 4-M

SEX: MALE

DOSE: 1.0 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8146	121	136	116	189	148	280
8156	368	343	386	354	390	283
8160	400	400	400	400	400	400
8144	214	384	303	400	400	400

MEAN	276	316	301	336	335	341
S.D.	131.3	122.2	130.7	100.2	124.4	68.4
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 1-F

SEX: FEMALE

DOSE: 0 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8211	129	201	326	400	213	325
8214	217	255	214	178	287	309
8184	245	156	400	400	400	400
8180	254	358	336	204	211	310

MEAN	211	243	319	296	278	336
S.D.	57.1	87.0	77.3	121.1	88.8	43.3
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 2-F

SEX: FEMALE

DOSE: 0.1 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8207	226	260	400	400	400	400
8206	184	315	400	400	400	207
8185	216	245	271	313	258	228
8199	400	229	325	400	311	329

MEAN	257	262	349	378	342	291
S.D.	97.3	37.4	62.9	43.5	70.1	90.1
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 3-F

SEX: FEMALE

DOSE: 0.3 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8215	123	400	169	192	400	374
8193	49	262	284	338	260	279
8181	259	190	400	400	400	274
8197	381	391	377	303	341	346

MEAN	203	311	308	308	350	318
S.D.	147.1	102.2	105.1	87.3	66.3	49.6
N	4	4	4	4	4	4

--: Data Unavailable

FOUR WEEK ORAL TOXICITY STUDY  
OF WR24511 IN DOGS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)

STUDY: 134

GROUP: 4-F

SEX: FEMALE

DOSE: 1.0 (mg base/kg/day)

ANIMAL # DAY -13 DAY -9 DAY 5 DAY 12 DAY 19 DAY 26

8196	268	294	223	251	224	315
8213	400	225	288	252	260	400
8194	243	337	330	322	324	319
8182	238	192	176	376	399	400

MEAN	287	262	254	300	302	359
S.D.	76.3	65.6	68.3	60.5	76.9	47.9
N	4	4	4	4	4	4

--: Data Unavailable

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APPENDIX 6

Individual Clinical Chemistry Data

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

Clinical Chemistry Test Directory

STUDY: 134

NO.	ABBR. UNITS	DESCRIPTION PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT---		---UPPER LIMIT---	
						MALE	FEMALE	MALE	FEMALE
1.	ALT U/L	Alanine Aminotransferase Integer	NO			20	20	60	60
2.	AST U/L	Aspartate Aminotransferase Integer	NO			20	20	60	60
3.	TP g/dL	Total Protein 0.0	NO			6.0	6.0	8.0	8.0
4.	ALB g/dL	Albumin 0.0	NO			2.7	2.7	3.7	3.7
5.	TBILI mg/dL	Total Bilirubin 0.00	NO			0.00	0.00	0.30	0.30
6.	ALKP U/L	Alkaline Phosphatase Integer	NO			50	50	200	200
7.	GGT U/L	Gamma Glutamyl Transferase Integer	NO			0	0	10	10
8.	CHOL mg/dL	Cholesterol Integer	NO			150	150	250	250
9.	TRY mg/dL	Triglycerides Integer	NO			20	20	60	60
10.	LDH U/L	Lactate Dehydrogenase Integer	NO			25	25	200	200
11.	CK U/L	Creatine Kinase Integer	NO			50	50	300	300
12.	BUN mg/dL	Blood Urea Nitrogen 0.0	NO			8.0	8.0	18.0	18.0
13.	CREA mg/dL	Creatinine 0.00	NO			0.50	0.50	1.00	1.00
14.	NA mmol/L	Sodium Integer	NO			140	140	150	150
15.	K mmol/L	Potassium 0.00	NO			4.00	4.00	5.25	5.25

(REPORT CONTINUED)

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Alanine Aminotransferase

STUDY ID: 134  
STUDY NO: 134  
ABBR: ALT

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	47	39	37	38
8214	30	28	35	34
8184	27	25	29	32
8180	25	25	21	23
MEAN	32	29	31	32
SD	10.0	6.7	7.2	6.3
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	46	44	44	47
8206	33	34	35	38
8185	63	39	32	54
8199	22	24	21	41
MEAN	41	35	33	45
SD	17.6	8.5	9.5	7.1
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	27	24	65	28
8193	47	43	46	46
8181	40	27	26	31
8197	30	31	41	39
MEAN	36	31	45	36
SD	9.2	8.3	16.1	8.1
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	27	24	21	20
8213	39	47	42	34
8194	48	39	48	44
8182	34	32	35	30
MEAN	37	36	37	32
SD	8.8	9.8	11.6	9.9
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Aspartate Aminotransferase

STUDY ID: 134  
STUDY NO: 134  
ABBR: AST

SEX: MALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	28	32	29	38
8143	32	32	30	40
8148	34	33	39	39
8153	34	33	31	44
MEAN	32	33	32	40
SD	2.8	0.6	4.6	2.6
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	37	37	39	47
8170	27	28	36	32
8147	34	35	43	40
8151	25	31	33	36
MEAN	31	33	38	39
SD	5.7	4.0	4.3	6.4
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	35	31	37	41
8159	31	28	35	44
8175	28	33	50	47
8166	28	30	39	37
MEAN	31	31	40	42
SD	3.3	2.1	6.7	4.3
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	39	40	46	47
8156	29	28	37	49
8160	35	40	43	61
8144	32	37	47	62
MEAN	34	36	43	55
SD	4.3	5.7	4.5	7.8
N	4	4	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Aspartate AminotransferaseSTUDY ID: 134  
STUDY NO: 134  
ABBR: AST

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	31	33	31	37
8214	28	26	29	50
8184	39	41	49	43
8180	32	32	38	41
MEAN	33	33	37	43
SD	4.7	6.2	9.0	5.4
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	33	37	44	33
8206	35	43	38	41
8185	38	27	28	42
8199	27	37	46	37
MEAN	33	36	39	38
SD	4.6	6.6	8.1	4.1
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	31	38	57	46
8193	33	36	37	36
8181	41	32	35	48
8197	24	32	68	37
MEAN	32	35	49	42
SD	7.0	3.0	16.0	6.1
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	28	33	45	36
8213	40	56	55	41
8194	28	33	40	40
8182	26	38	59	45
MEAN	31	40	50	41
SD	6.4	10.9	8.8	3.7
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Total Protein

STUDY ID: 134  
STUDY NO: 134  
ABBR: TP

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	6.3	5.9	6.7	6.3
8143	6.1	5.9	6.8	6.6
8148	6.1	6.5	6.0	6.5
8153	6.6	5.9	6.3	6.8
MEAN	6.3	6.1	6.5	6.6
SD	0.24	0.30	0.37	0.21
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	6.6	6.3	7.0	6.9
8170	6.6	6.4	6.4	6.4
8147	5.9	6.1	6.8	6.4
8151	5.6	6.7	6.6	6.2
MEAN	6.2	6.4	6.7	6.5
SD	0.51	0.25	0.26	0.30
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	6.3	5.9	6.5	6.5
8159	5.8	6.2	6.3	6.3
8175	6.0	6.1	6.8	6.7
8166	5.4	6.1	6.1	6.4
MEAN	5.9	6.1	6.4	6.5
SD	0.38	0.13	0.30	0.17
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	5.9	5.6	6.1	6.7
8156	6.7	6.8	7.3	7.1
8160	5.6	6.0	6.2	6.4
8144	5.8	6.0	6.8	6.6
MEAN	6.0	6.1	6.6	6.7
SD	0.48	0.50	0.56	0.29
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Total Protein

STUDY ID: 134  
STUDY NO: 134  
ABBR: TP

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	6.0	6.1	6.7	6.3
8214	5.8	5.3	6.1	5.7
8184	6.9	6.2	7.5	6.7
8180	5.9	6.0	7.1	5.9
MEAN	6.2	5.9	6.9	6.2
SD	0.51	0.41	0.60	0.44
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	5.9	6.3	6.6	6.4
8206	6.1	5.5	7.2	6.3
8185	6.4	6.1	7.0	6.9
8199	6.0	6.1	6.2	6.6
MEAN	6.1	6.0	6.8	6.6
SD	0.22	0.35	0.44	0.26
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	5.4	6.1	7.0	6.4
8193	6.2	6.3	6.6	6.6
8181	6.3	6.2	6.2	6.3
8197	5.6	6.3	7.3	6.2
MEAN	5.9	6.2	6.8	6.4
SD	0.44	0.10	0.48	0.17
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	6.1	5.7	6.4	6.4
8213	5.8	6.3	6.4	6.0
8194	6.0	6.3	6.4	6.4
8182	6.4	5.8	6.7	6.3
MEAN	6.1	6.0	6.5	6.3
SD	0.25	0.32	0.15	0.19
N	4	4	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: AlbuminSTUDY ID: 134  
STUDY NO: 134  
ABBR: ALB

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	3.5	3.0	3.0	3.3
8143	3.3	3.3	3.1	3.4
8148	3.2	3.4	3.0	3.6
8153	3.3	3.4	3.3	3.5
MEAN	3.3	3.3	3.1	3.5
SD	0.13	0.19	0.14	0.13
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	3.7	3.1	3.2	3.6
8170	3.7	3.2	3.1	3.3
8147	3.3	3.5	3.5	3.4
8151	3.0	3.3	3.2	3.3
MEAN	3.4	3.3	3.3	3.4
SD	0.34	0.17	0.17	0.14
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	3.4	3.3	3.3	3.3
8159	3.2	3.2	3.1	3.2
8175	3.4	3.3	3.1	3.4
8166	3.0	3.2	3.1	3.4
MEAN	3.3	3.3	3.2	3.3
SD	0.19	0.06	0.10	0.10
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	3.2	2.8	3.2	2.9
8156	3.5	3.3	3.4	3.2
8160	3.2	3.0	3.6	3.0
8144	3.0	3.2	3.0	2.8
MEAN	3.2	3.1	3.3	3.0
SD	0.21	0.22	0.26	0.17
N	4	4	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: AlbuminSTUDY ID: 134  
STUDY NO: 134  
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
-----------	---------	----------	--------	--------

GROUP: 1-F:0 mg base/kg/day

8211	3.1	3.2	3.2	3.4
8214	3.1	2.8	3.0	3.1
8184	3.6	3.3	3.4	3.4
8180	3.1	3.2	3.2	3.2

MEAN	3.2	3.1	3.2	3.3
SD	0.25	0.22	0.16	0.15
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	3.1	3.3	3.6	3.4
8206	3.2	3.1	3.2	3.4
8185	3.5	3.1	3.3	3.4
8199	2.9	3.2	3.2	3.4

MEAN	3.2	3.2	3.3	3.4
SD	0.25	0.10	0.19	0.00
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	3.0	3.3	3.3	3.4
8193	3.4	3.2	3.5	3.4
8181	3.3	3.2	3.1	3.4
8197	3.1	3.1	3.4	3.3

MEAN	3.2	3.2	3.3	3.4
SD	0.18	0.08	0.17	0.05
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	3.3	3.2	3.3	3.0
8213	2.9	3.3	3.1	2.7
8194	3.1	3.1	3.2	2.9
8182	3.5	3.3	3.2	3.1

MEAN	3.2	3.2	3.2	2.9
SD	0.26	0.10	0.08	0.17
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Globulin

STUDY ID: 134  
STUDY NO: 134  
ABBR: GLOB

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	2.8	2.9	3.7	3.0
8143	2.8	2.6	3.7	3.2
8148	2.9	3.1	3.0	2.9
8153	3.3	2.5	3.0	3.3
MEAN	3.0	2.8	3.4	3.1
SD	0.24	0.28	0.40	0.18
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	2.9	3.2	3.8	3.3
8170	2.9	3.2	3.3	3.1
8147	2.6	2.6	3.3	3.0
8151	2.6	3.4	3.4	2.9
MEAN	2.8	3.1	3.5	3.1
SD	0.17	0.35	0.24	0.17
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	2.9	2.6	3.2	3.2
8159	2.6	3.0	3.2	3.1
8175	2.6	2.8	3.7	3.3
8166	2.4	2.9	3.0	3.0
MEAN	2.6	2.8	3.3	3.2
SD	0.21	0.17	0.30	0.13
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	2.7	2.8	2.9	3.8
8156	3.2	3.5	3.9	3.9
8160	2.4	3.0	2.6	3.4
8144	2.8	2.8	3.8	3.8
MEAN	2.8	3.0	3.3	3.7
SD	0.33	0.33	0.65	0.22
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: GlobulinSTUDY ID: 134  
STUDY NO: 134  
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
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GROUP: 1-F:0 mg base/kg/day

8211	2.9	2.9	3.5	2.9
8214	2.7	2.5	3.1	2.6
8184	3.3	2.9	4.1	3.3
8180	2.8	2.8	3.9	2.7

MEAN	2.9	2.8	3.7	2.9
SD	0.26	0.19	0.44	0.31
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	2.8	3.0	3.0	3.0
8206	2.9	2.4	4.0	2.9
8185	2.9	3.0	3.7	3.5
8199	3.1	2.9	3.0	3.2

MEAN	2.9	2.8	3.4	3.2
SD	0.13	0.29	0.51	0.26
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	2.4	2.8	3.7	3.0
8193	2.8	3.1	3.1	3.2
8181	3.0	3.0	3.1	2.9
8197	2.5	3.2	3.9	2.9

MEAN	2.7	3.0	3.5	3.0
SD	0.28	0.17	0.41	0.14
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	2.8	2.5	3.1	3.4
8213	2.9	3.0	3.3	3.3
8194	2.9	3.2	3.2	3.5
8182	2.9	2.5	3.5	3.2

MEAN	2.9	2.8	3.3	3.4
SD	0.05	0.36	0.17	0.13
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: A/G Ratio

STUDY ID: 134  
STUDY NO: 134  
ABBR: A/G

SEX: MALE

UNITS: -

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	1.25	1.03	0.81	1.10
8143	1.18	1.27	0.84	1.06
8148	1.10	1.10	1.00	1.24
8153	1.00	1.36	1.10	1.06
MEAN	1.13	1.19	0.94	1.12
SD	0.108	0.152	0.137	0.085
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	1.28	0.97	0.84	1.09
8170	1.28	1.00	0.94	1.06
8147	1.27	1.35	1.06	1.13
8151	1.15	0.97	0.94	1.14
MEAN	1.25	1.07	0.95	1.11
SD	0.064	0.186	0.090	0.037
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	1.17	1.27	1.03	1.03
8159	1.23	1.07	0.97	1.03
8175	1.31	1.18	0.84	1.03
8166	1.25	1.10	1.03	1.13
MEAN	1.24	1.16	0.97	1.06
SD	0.058	0.090	0.090	0.050
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	1.19	1.00	1.10	0.76
8156	1.09	0.94	0.87	0.82
8160	1.33	1.00	1.38	0.88
8144	1.07	1.14	0.79	0.74
MEAN	1.17	1.02	1.04	0.80
SD	0.119	0.085	0.265	0.063
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: A/G Ratio

STUDY ID: 134  
STUDY NO: 134  
ABBR: A/G

SEX: FEMALE

UNITS: -

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	1.07	1.10	0.91	1.17
8214	1.15	1.12	0.97	1.19
8184	1.09	1.14	0.83	1.03
8180	1.11	1.14	0.82	1.19
MEAN	1.11	1.13	0.88	1.15
SD	0.034	0.019	0.071	0.077
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	1.11	1.10	1.20	1.13
8206	1.10	1.29	0.80	1.17
8185	1.21	1.03	0.89	0.97
8199	0.94	1.10	1.07	1.06
MEAN	1.09	1.13	0.99	1.08
SD	0.112	0.112	0.179	0.088
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	1.25	1.18	0.89	1.13
8193	1.21	1.03	1.13	1.06
8181	1.10	1.07	1.00	1.17
8197	1.24	0.97	0.87	1.14
MEAN	1.20	1.06	0.97	1.13
SD	0.069	0.088	0.120	0.047
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	1.18	1.28	1.06	0.88
8213	1.00	1.10	0.94	0.82
8194	1.07	0.97	1.00	0.83
8182	1.21	1.32	0.91	0.97
MEAN	1.12	1.17	0.98	0.88
SD	0.097	0.163	0.067	0.069
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Total Bilirubin

STUDY ID: 134  
STUDY NO: 134  
ABBR: TBILI

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.14	0.17	0.17	0.18
8143	0.15	0.13	0.11	0.19
8148	0.13	0.12	0.12	0.16
8153	0.13	0.10	0.13	0.15
MEAN	0.14	0.13	0.13	0.17
SD	0.010	0.029	0.026	0.018
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	0.13	0.12	0.14	0.17
8170	0.15	0.13	0.13	0.14
8147	0.14	0.12	0.12	0.20
8151	0.14	0.14	0.13	0.15
MEAN	0.14	0.13	0.13	0.17
SD	0.008	0.010	0.008	0.026
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	0.14	0.10	0.15	0.24
8159	0.15	0.14	0.17	0.15
8175	0.12	0.14	0.23	0.16
8166	0.11	0.13	0.14	0.16
MEAN	0.13	0.13	0.17	0.18
SD	0.018	0.019	0.040	0.042
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	0.14	0.11	0.15	0.17
8156	0.12	0.09	0.14	0.17
8160	0.13	0.12	0.15	0.14
8144	0.11	0.12	0.13	0.15
MEAN	0.13	0.11	0.14	0.16
SD	0.013	0.014	0.010	0.015
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Total BilirubinSTUDY ID: 134  
STUDY NO: 134  
ABBR: TBILI

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.12	0.14	0.13	0.14
8214	0.10	0.09	0.14	0.16
8184	0.14	0.15	0.18	0.14
8180	0.10	0.12	0.12	0.14
MEAN	0.12	0.13	0.14	0.15
SD	0.019	0.026	0.026	0.010
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.13	0.15	0.19	0.17
8206	0.12	0.13	0.15	0.17
8185	0.14	0.16	0.20	0.24
8199	0.10	0.09	0.15	0.18
MEAN	0.12	0.13	0.17	0.19
SD	0.017	0.031	0.026	0.034
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.13	0.15	0.13	0.23
8193	0.16	0.16	0.21	0.21
8181	0.14	0.13	0.15	0.25
8197	0.09	0.10	0.30	0.14
MEAN	0.13	0.14	0.20	0.21
SD	0.029	0.026	0.076	0.048
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.13	0.11	0.19	0.15
8213	0.11	0.16	0.17	0.13
8194	0.15	0.12	0.22	0.17
8182	0.16	0.15	0.37	0.15
MEAN	0.14	0.14	0.24	0.15
SD	0.022	0.024	0.091	0.016
N	4	4	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Alkaline Phosphatase

STUDY ID: 134  
STUDY NO: 134  
ABBR: ALKP

SEX: MALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	158	140	141	128
8143	129	124	142	169
8148	120	125	113	103
8153	146	138	149	133
MEAN	138	132	136	133
SD	17.0	8.4	15.9	27.2
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	226	200	222	180
8170	176	163	198	152
8147	256	269	235	181
8151	139	166	128	115
MEAN	199	200	196	157
SD	52.0	49.3	47.7	31.1
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	144	139	129	103
8159	101	77	86	65
8175	110	102	102	94
8166	139	133	141	111
MEAN	124	113	115	93
SD	21.2	28.8	25.0	20.1
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	111	99	96	92
8156	147	159	135	146
8160	116	111	115	96
8144	105	107	136	132
MEAN	120	119	121	117
SD	18.7	27.1	19.0	26.7
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Alkaline Phosphatase

STUDY ID: 134  
STUDY NO: 134  
ABBR: ALKP

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	148	139	142	109
8214	116	97	109	85
8184	113	91	116	133
8180	102	115	106	66
MEAN	120	111	118	98
SD	19.8	21.6	16.4	29.1
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	348	278	274	256
8206	231	211	209	189
8185	91	78	103	67
8199	114	108	129	108
MEAN	196	169	179	155
SD	118.4	92.5	77.9	84.3
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	124	117	150	81
8193	129	128	125	112
8181	129	118	118	97
8197	84	92	104	78
MEAN	117	114	124	92
SD	21.8	15.3	19.3	15.7
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	120	112	114	101
8213	98	98	86	102
8194	88	95	94	107
8182	123	119	124	84
MEAN	107	106	105	99
SD	17.0	11.4	17.5	10.0
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Gamma Glutamyl Transferase

STUDY ID: 134  
STUDY NO: 134  
ABBR: GGT

SEX: MALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	2	3	4	4
8143	3	2	4	2
8148	5	5	5	5
8153	4	3	2	3
MEAN	4	3	4	4
SD	1.3	1.3	1.3	1.3
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	3	4	4	2
8170	5	3	4	4
8147	4	3	4	3
8151	3	4	5	3
MEAN	4	4	4	3
SD	1.0	0.6	0.5	0.8
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	2	3	3	4
8159	3	2	3	3
8175	3	3	2	5
8166	4	4	6	6
MEAN	3	3	4	5
SD	0.8	0.8	1.7	1.3
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	3	3	4	4
8156	5	1	5	2
8160	3	4	5	2
8144	3	3	4	4
MEAN	4	3	5	3
SD	1.0	1.3	0.6	1.2
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Gamma Glutamyl Transferase

STUDY ID: 134  
STUDY NO: 134  
ABBR: GGT

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	3	3	4	3
8214	3	2	4	6
8184	6	4	1	3
8180	2	3	2	2
MEAN	4	3	3	4
SD	1.7	0.8	1.5	1.7
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	8	5	7	4
8206	3	3	2	2
8185	3	2	4	0
8199	3	4	2	4
MEAN	4	4	4	3
SD	2.5	1.3	2.4	1.9
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	4	3	6	1
8193	3	2	3	3
8181	1	2	2	2
8197	4	3	4	1
MEAN	3	3	4	2
SD	1.4	0.6	1.7	1.0
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	4	2	4	4
8213	3	3	4	3
8194	4	2	4	4
8182	3	3	5	2
MEAN	4	3	4	3
SD	0.6	0.6	0.5	1.0
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Cholesterol

STUDY ID: 134  
STUDY NO: 134  
ABBR: CHOL

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	170	165	189	191
8143	176	163	178	169
8148	196	223	184	190
8153	255	183	192	188
MEAN	199	184	186	185
SD	38.8	27.8	6.1	10.4
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	209	207	210	202
8170	214	193	192	194
8147	156	143	174	170
8151	161	222	189	182
MEAN	185	191	191	187
SD	30.7	34.3	14.8	14.0
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	173	169	158	160
8159	200	220	197	175
8175	154	183	213	222
8166	201	211	220	196
MEAN	182	196	197	188
SD	22.7	23.8	27.7	26.9
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	170	144	196	202
8156	233	222	257	270
8160	172	163	175	200
8144	155	168	206	186
MEAN	183	174	209	215
SD	34.5	33.5	34.8	37.7
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Cholesterol

STUDY ID: 134  
STUDY NO: 134  
ABBR: CHOL

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	188	210	215	198
8214	148	150	175	151
8184	227	172	238	243
8180	166	157	180	139
MEAN	182	172	202	183
SD	34.0	26.8	29.9	47.6
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	161	166	167	163
8206	118	123	148	133
8185	189	195	219	226
8199	159	154	143	169
MEAN	157	160	169	173
SD	29.2	29.8	34.7	38.8
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	155	166	212	208
8193	155	146	165	185
8181	157	164	149	142
8197	164	172	210	193
MEAN	158	162	184	182
SD	4.3	11.2	31.9	28.3
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	169	162	172	172
8213	142	160	169	154
8194	227	210	225	224
8182	187	206	261	246
MEAN	181	185	207	199
SD	35.7	27.2	44.4	43.2
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Triglycerides

STUDY ID: 134  
STUDY NO: 134  
ABBR: TRY

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	38	51	48	26
8143	46	34	34	43
8148	30	58	25	20
8153	48	35	32	37
MEAN	41	45	35	32
SD	8.2	11.9	9.6	10.4
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	43	29	35	37
8170	37	38	21	21
8147	50	29	32	35
8151	36	36	35	29
MEAN	42	33	31	31
SD	6.5	4.7	6.7	7.2
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	37	32	35	31
8159	44	46	46	42
8175	35	35	78	34
8166	35	45	31	32
MEAN	38	40	48	35
SD	4.3	7.0	21.3	5.0
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	44	26	37	46
8156	36	33	44	64
8160	31	29	35	48
8144	46	55	58	61
MEAN	39	36	44	55
SD	7.0	13.1	10.4	9.1
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Triglycerides

STUDY ID: 134

SEX: FEMALE

STUDY NO: 134

ABBR: TRY

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
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GROUP: 1-F:0 mg base/kg/day

8211	49	53	48	39
8214	36	39	53	46
8184	32	33	46	30
8180	41	39	41	39
MEAN	40	41	47	39
SD	7.3	8.5	5.0	6.6
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	37	39	43	31
8206	26	21	39	32
8185	62	52	59	52
8199	35	24	45	41
MEAN	40	34	47	39
SD	15.4	14.4	8.7	9.8
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	32	45	75	46
8193	43	51	66	54
8181	36	41	32	39
8197	33	31	99	34
MEAN	36	42	68	43
SD	5.0	8.4	27.7	8.7
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	27	45	60	40
8213	42	68	55	32
8194	30	42	40	48
8182	39	46	77	45
MEAN	35	50	58	41
SD	7.1	12.0	15.3	7.0
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Lactate DehydrogenaseSTUDY ID: 134  
STUDY NO: 134  
ABBR: LDH

SEX: MALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
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GROUP: 1-M:0 mg base/kg/day

8172	56	50	45	81
8143	51	44	30	55
8148	62	26	77	50
8153	117	68	51	95
MEAN	72	47	51	70
SD	30.7	17.3	19.6	21.4
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	109	60	129	262
8170	71	38	80	69
8147	53	100	57	60
8151	44	53	51	64
MEAN	69	63	79	114
SD	28.8	26.5	35.4	98.9
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	62	56	40	55
8159	56	40	50	86
8175	49	91	175	56
8166	42	48	47	51
MEAN	52	59	78	62
SD	8.7	22.5	64.8	16.1
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	68	67	72	139
8156	42	82	49	193
8160	52	55	44	128
8144	52	53	67	120
MEAN	54	64	58	145
SD	10.8	13.4	13.6	32.9
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Lactate Dehydrogenase

STUDY ID: 134  
STUDY NO: 134  
ABBR: LDH

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	47	71	39	58
8214	53	133	59	175
8184	71	62	111	75
8180	199	162	234	378
MEAN	93	107	111	172
SD	71.7	48.4	87.6	147.0
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	69	63	111	59
8206	40	86	81	59
8185	30	38	45	115
8199	110	118	114	110
MEAN	62	76	88	86
SD	35.9	34.0	32.2	31.0
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	43	69	161	114
8193	47	121	53	85
8181	128	67	88	184
8197	27	49	86	34
MEAN	61	77	97	104
SD	45.3	31.0	45.6	62.6
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	40	48	46	37
8213	60	117	105	90
8194	70	110	65	109
8182	52	113	221	149
MEAN	56	97	109	96
SD	12.7	32.8	78.5	46.5
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Creatine Kinase

STUDY ID: 134  
STUDY NO: 134  
ABBR: CK

SEX: MALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	171	225	182	154
8143	404	270	154	330
8148	205	108	215	138
8153	568	235	213	197
MEAN	337	210	191	205
SD	185.1	70.4	28.9	87.1
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	254	253	217	440
8170	191	147	250	188
8147	221	287	309	179
8151	159	165	161	127
MEAN	206	213	234	234
SD	40.7	67.7	61.9	140.3
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	235	162	172	149
8159	175	102	165	154
8175	131	281	369	195
8166	145	137	156	114
MEAN	172	171	216	153
SD	46.1	77.7	102.5	33.2
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	297	285	145	161
8156	158	204	116	363
8160	184	182	149	129
8144	204	162	143	194
MEAN	211	208	138	212
SD	60.5	54.0	15.0	104.3
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Creatine KinaseSTUDY ID: 134  
STUDY NO: 134  
ABBR: CK

SEX: FEMALE

UNITS: U/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
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GROUP: 1-F:0 mg base/kg/day

8211	158	288	180	343
8214	190	175	148	774
8184	309	288	313	189
8180	222	212	230	290
MEAN	220	241	218	399
SD	65.0	56.6	71.9	258.0
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	231	230	370	145
8206	164	285	207	180
8185	133	122	151	187
8199	155	208	244	166
MEAN	171	211	243	170
SD	42.2	67.7	92.9	18.5
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	183	263	200	229
8193	209	244	174	188
8181	351	133	236	237
8197	160	164	371	113
MEAN	226	201	245	192
SD	85.9	62.4	87.6	56.7
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	158	178	163	87
8213	183	555	180	123
8194	172	185	135	118
8182	152	510	251	172
MEAN	166	357	182	125
SD	14.0	203.5	49.4	35.1
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Blood Urea Nitrogen

STUDY ID: 134  
STUDY NO: 134  
ABBR: BUN

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	12.0	14.6	13.5	15.7
8143	14.2	14.6	15.1	12.7
8148	11.5	17.9	11.1	11.5
8153	16.9	12.5	15.8	14.0
MEAN	13.7	14.9	13.9	13.5
SD	2.46	2.23	2.09	1.80
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	16.8	16.0	16.1	20.6
8170	12.8	14.2	14.3	11.7
8147	16.1	14.2	15.3	19.6
8151	13.4	15.5	15.4	20.0
MEAN	14.8	15.0	15.3	18.0
SD	1.97	0.92	0.74	4.20
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	16.7	11.2	14.3	18.1
8159	15.1	15.8	14.4	12.8
8175	11.8	14.9	14.5	14.1
8166	8.3	11.1	11.1	19.4
MEAN	13.0	13.3	13.6	16.1
SD	3.73	2.45	1.65	3.15
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	13.4	11.6	13.3	15.2
8156	14.3	14.6	14.6	13.7
8160	16.1	16.0	13.7	14.3
8144	18.7	18.5	15.1	20.2
MEAN	15.6	15.2	14.2	15.9
SD	2.34	2.88	0.82	2.96
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Blood Urea Nitrogen

STUDY ID: 134  
STUDY NO: 134  
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	15.1	13.6	15.4	16.0
8214	14.2	16.1	15.0	17.3
8184	17.7	16.7	21.9	16.7
8180	11.0	10.1	11.5	11.5
MEAN	14.5	14.1	16.0	15.4
SD	2.77	3.00	4.34	2.64
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	13.1	13.7	17.3	20.0
8206	14.4	11.9	12.6	17.9
8185	16.0	12.2	16.5	20.1
8199	9.4	13.6	15.5	14.5
MEAN	13.2	12.9	15.5	18.1
SD	2.81	0.93	2.05	2.62
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	9.1	9.9	14.0	14.9
8193	12.1	10.9	12.1	12.4
8181	14.0	13.7	12.9	12.7
8197	13.6	11.3	19.3	20.6
MEAN	12.2	11.5	14.6	15.2
SD	2.22	1.61	3.24	3.80
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	15.2	12.9	16.8	16.0
8213	11.8	15.4	12.9	14.5
8194	12.9	13.3	15.0	15.4
8182	18.1	16.0	19.9	20.0
MEAN	14.5	14.4	16.2	16.5
SD	2.79	1.53	2.96	2.43
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: CreatinineSTUDY ID: 134  
STUDY NO: 134  
ABBR: CREA

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.79	0.85	0.86	0.81
8143	0.72	0.77	0.74	0.76
8148	0.59	0.64	0.69	0.74
8153	0.71	0.78	0.77	0.75
MEAN	0.70	0.76	0.77	0.77
SD	0.083	0.088	0.071	0.031
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	0.81	0.87	0.90	0.91
8170	0.66	0.67	0.68	0.75
8147	0.76	0.82	0.92	0.93
8151	0.71	0.81	0.78	0.80
MEAN	0.74	0.79	0.82	0.85
SD	0.065	0.086	0.112	0.087
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	0.73	0.67	0.84	0.81
8159	0.72	0.69	0.75	0.76
8175	0.79	0.72	0.75	0.80
8166	0.63	0.69	0.78	0.80
MEAN	0.72	0.69	0.78	0.79
SD	0.066	0.021	0.042	0.022
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	0.73	0.80	0.85	0.86
8156	0.78	0.77	0.90	0.83
8160	0.60	0.65	0.73	0.74
8144	0.64	0.65	0.74	0.77
MEAN	0.69	0.72	0.81	0.80
SD	0.082	0.079	0.083	0.055
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Creatinine

STUDY ID: 134  
STUDY NO: 134  
ABBR: CREA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.81	0.73	0.83	0.88
8214	0.73	0.66	0.72	0.73
8184	0.73	0.67	0.63	0.59
8180	0.64	0.67	0.65	0.67
MEAN	0.73	0.68	0.71	0.72
SD	0.069	0.032	0.090	0.123
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.61	0.69	0.72	0.64
8206	0.73	0.71	0.71	0.78
8185	0.79	0.71	0.81	0.74
8199	0.68	0.75	0.78	0.82
MEAN	0.70	0.72	0.76	0.75
SD	0.076	0.025	0.048	0.077
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.74	0.75	0.70	0.81
8193	0.74	0.67	0.72	0.67
8181	0.67	0.73	0.72	0.74
8197	0.70	0.76	0.96	0.79
MEAN	0.71	0.73	0.78	0.75
SD	0.034	0.040	0.124	0.062
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.73	0.69	0.85	0.79
8213	0.61	0.63	0.67	0.64
8194	0.73	0.67	0.84	0.76
8182	0.75	0.74	0.79	0.77
MEAN	0.71	0.68	0.79	0.74
SD	0.064	0.046	0.083	0.068
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Sodium

STUDY ID: 134  
STUDY NO: 134  
ABBR: NA

SEX: MALE

UNITS: mmol/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	144	145	146	144
8143	142	144	143	141
8148	143	145	143	144
8153	146	144	144	143
MEAN	144	145	144	143
SD	1.7	0.6	1.4	1.4
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	143	147	145	145
8170	145	145	143	145
8147	143	145	147	147
8151	144	147	145	146
MEAN	144	146	145	146
SD	1.0	1.2	1.6	1.0
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	145	144	144	144
8159	143	144	144	142
8175	144	145	142	145
8166	144	145	146	146
MEAN	144	145	144	144
SD	0.8	0.6	1.6	1.7
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	143	143	144	144
8156	146	149	149	146
8160	145	146	144	147
8144	142	145	143	144
MEAN	144	146	145	145
SD	1.8	2.5	2.7	1.5
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: SodiumSTUDY ID: 134  
STUDY NO: 134  
ABBR: NA

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	141	145	144	144
8214	146	145	144	143
8184	146	143	147	143
8180	144	145	147	145
MEAN	144	145	146	144
SD	2.4	1.0	1.7	1.0
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	144	145	147	144
8206	144	143	143	144
8185	145	145	145	145
8199	144	144	144	145
MEAN	144	144	145	145
SD	0.5	1.0	1.7	0.6
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	145	145	145	146
8193	143	142	144	142
8181	145	147	145	143
8197	141	143	143	145
MEAN	144	144	144	144
SD	1.9	2.2	1.0	1.8
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	145	143	144	144
8213	144	144	144	143
8194	145	144	144	144
8182	141	146	145	144
MEAN	144	144	144	144
SD	1.9	1.3	0.5	0.5
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Potassium

STUDY ID: 134  
STUDY NO: 134  
ABBR: K

SEX: MALE

UNITS: mmol/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	4.54	4.47	4.90	4.16
8143	4.82	4.83	4.81	4.64
8148	4.73	4.58	4.18	4.15
8153	5.06	4.84	4.79	4.37
MEAN	4.79	4.68	4.67	4.33
SD	0.216	0.185	0.330	0.230
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	4.58	4.57	4.58	5.52
8170	4.65	4.42	4.28	4.32
8147	4.33	4.43	4.27	4.47
8151	4.44	4.73	4.27	4.20
MEAN	4.50	4.54	4.35	4.63
SD	0.143	0.145	0.153	0.605
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	4.64	4.02	4.62	4.34
8159	4.34	4.45	3.95	4.49
8175	4.32	4.62	4.28	4.07
8166	4.54	4.54	4.92	4.08
MEAN	4.46	4.41	4.44	4.25
SD	0.156	0.268	0.420	0.206
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	4.79	4.64	4.57	4.71
8156	4.64	4.87	4.64	4.67
8160	4.33	4.63	4.19	3.99
8144	4.42	4.44	4.19	4.12
MEAN	4.55	4.65	4.40	4.37
SD	0.209	0.176	0.241	0.371
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: PotassiumSTUDY ID: 134  
STUDY NO: 134  
ABBR: K

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	4.05	4.26	3.98	4.34
8214	4.38	4.87	4.47	4.48
8184	5.14	4.27	4.58	4.27
8180	4.45	4.50	4.21	4.73
MEAN	4.51	4.48	4.31	4.46
SD	0.458	0.286	0.269	0.203
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	4.29	4.42	4.66	4.18
8206	4.92	4.63	4.10	4.23
8185	4.61	4.98	4.59	4.50
8199	4.52	4.34	4.13	4.52
MEAN	4.59	4.59	4.37	4.36
SD	0.261	0.286	0.296	0.177
N	4	4	4	4

GROUP: 3-F:D.3 mg base/kg/day				
8215	4.71	4.63	4.62	4.92
8193	4.24	4.15	4.32	4.31
8181	4.66	4.59	4.39	4.49
8197	4.03	4.75	4.33	4.15
MEAN	4.41	4.53	4.42	4.47
SD	0.330	0.262	0.140	0.332
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	4.70	4.55	3.89	4.46
8213	4.26	4.54	4.35	3.81
8194	4.41	4.42	4.37	4.39
8182	4.21	3.97	4.62	4.35
MEAN	4.40	4.37	4.31	4.25
SD	0.220	0.273	0.304	0.298
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Chloride

STUDY ID: 134  
STUDY NO: 134  
ABBR: CL

SEX: MALE

UNITS: mEq/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	116	112	115	115
8143	119	121	116	120
8148	124	121	117	118
8153	123	123	115	119
MEAN	121	119	116	118
SD	3.7	4.9	1.0	2.2
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	117	124	115	119
8170	112	118	114	117
8147	124	121	116	122
8151	121	117	114	115
MEAN	119	120	115	118
SD	5.2	3.2	1.0	3.0
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	115	125	116	115
8159	115	121	115	113
8175	115	113	116	119
8166	120	112	116	118
MEAN	116	118	116	116
SD	2.5	6.3	0.5	2.8
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	118	122	122	117
8156	123	128	112	117
8160	120	122	115	121
8144	119	110	120	119
MEAN	120	121	117	119
SD	2.2	7.5	4.6	1.9
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Chloride

STUDY ID: 134  
STUDY NO: 134  
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	114	123	114	117
8214	122	120	120	119
8184	118	118	119	115
8180	117	120	121	116
MEAN	118	120	119	117
SD	3.3	2.1	3.1	1.7
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	120	129	111	120
8206	118	113	119	115
8185	122	115	114	118
8199	117	121	114	116
MEAN	119	120	115	117
SD	2.2	7.2	3.3	2.2
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	118	115	119	120
8193	119	127	116	115
8181	113	112	117	114
8197	114	127	118	116
MEAN	116	120	118	116
SD	2.9	7.9	1.3	2.6
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	121	118	119	118
8213	116	124	116	117
8194	120	122	116	113
8182	114	122	119	116
MEAN	118	122	118	116
SD	3.3	2.5	1.7	2.2
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Calcium

STUDY IO: 134  
STUDY NO: 134  
ABBR: CA

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	11.3	10.8	10.8	10.7
8143	10.9	11.0	11.0	10.6
8148	10.7	10.6	10.3	10.3
8153	11.5	11.0	11.1	10.8
MEAN	11.1	10.9	10.8	10.6
SD	0.37	0.19	0.36	0.22
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	11.5	11.6	11.1	10.9
8170	11.8	10.5	10.6	10.8
8147	11.0	10.6	10.8	10.7
8151	11.0	11.3	10.9	10.6
MEAN	11.3	11.0	10.9	10.8
SD	0.39	0.54	0.21	0.13
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	11.4	10.8	10.7	10.7
8159	11.3	11.0	10.7	10.7
8175	11.1	10.2	10.2	10.6
8166	10.6	10.4	10.6	10.9
MEAN	11.1	10.6	10.6	10.7
SD	0.36	0.37	0.24	0.13
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	10.6	10.6	10.6	10.4
8156	11.1	11.0	10.9	10.8
8160	10.8	10.2	10.2	10.2
8144	10.7	10.4	10.6	10.4
MEAN	10.8	10.6	10.6	10.5
SD	0.22	0.34	0.29	0.25
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSIND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: CalciumSTUDY IO: 134  
STUDY NO: 134  
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	10.7	11.0	10.6	11.2
8214	10.9	10.9	10.6	10.4
8184	11.6	10.7	10.5	10.5
8180	10.8	10.2	10.3	10.3
MEAN	11.0	10.7	10.5	10.6
SD	0.41	0.36	0.14	0.41
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	11.2	10.8	11.0	11.0
8206	11.1	10.6	10.6	10.7
8185	11.6	10.5	10.8	11.0
8199	11.0	10.6	10.5	10.8
MEAN	11.2	10.6	10.7	10.9
SD	0.26	0.13	0.22	0.15
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	10.8	10.6	11.1	11.1
8193	11.2	10.8	10.6	10.9
8181	11.2	10.4	10.8	10.4
8197	10.9	10.5	10.3	10.6
MEAN	11.0	10.6	10.7	10.8
SD	0.21	0.17	0.34	0.31
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	11.5	10.8	10.7	10.9
8213	10.8	10.7	10.6	10.4
8194	11.3	10.9	10.6	10.3
8182	10.5	10.0	10.1	10.0
MEAN	11.0	10.6	10.5	10.4
SD	0.46	0.41	0.27	0.37
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Inorganic Phosphorus

STUDY ID: 134  
STUDY NO: 134  
ABBR: IP

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	5.9	6.3	6.6	5.7
8143	6.0	6.3	6.6	5.6
8148	6.7	7.3	6.5	5.9
8153	5.6	6.5	6.4	6.1
MEAN	6.1	6.6	6.5	5.8
SD	0.47	0.48	0.10	0.22
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	6.0	6.7	6.5	5.5
8170	6.8	7.0	6.6	5.8
8147	5.9	5.4	5.2	5.7
8151	5.3	6.0	5.8	5.7
MEAN	6.0	6.3	6.0	5.7
SD	0.62	0.72	0.66	0.13
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	5.5	5.3	6.3	5.6
8159	5.2	6.5	5.7	5.9
8175	5.7	6.4	4.2	6.4
8166	5.7	6.1	5.6	6.1
MEAN	5.5	6.1	5.5	6.0
SD	0.24	0.54	0.89	0.34
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	5.1	4.8	5.8	4.7
8156	6.1	6.3	6.3	5.5
8160	6.3	6.2	5.6	5.1
8144	5.8	6.1	6.2	5.9
MEAN	5.8	5.9	6.0	5.3
SD	0.53	0.70	0.33	0.52
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Inorganic Phosphorus

STUDY ID: 134  
STUDY NO: 134  
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	4.6	4.7	4.9	5.2
8214	5.1	5.1	5.8	4.4
8184	6.9	5.7	6.5	6.3
8180	5.7	5.7	5.7	5.6
MEAN	5.6	5.3	5.7	5.4
SD	0.99	0.49	0.66	0.79
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	4.2	5.4	5.9	4.9
8206	6.0	7.1	6.3	6.3
8185	5.2	5.7	5.3	4.0
8199	5.0	5.6	5.5	4.7
MEAN	5.1	6.0	5.8	5.0
SD	0.74	0.78	0.44	0.96
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	5.4	5.3	5.0	4.2
8193	4.5	4.2	5.0	4.4
8181	5.3	6.4	5.8	4.8
8197	5.4	6.1	3.9	5.1
MEAN	5.2	5.5	4.9	4.6
SD	0.44	0.98	0.78	0.40
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	6.1	6.7	5.7	6.0
8213	5.6	5.3	5.8	5.1
8194	5.4	5.3	5.7	5.8
8182	5.1	4.8	4.6	5.5
MEAN	5.6	5.5	5.5	5.6
SD	0.42	0.82	0.57	0.39
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Glucose

STUDY ID: 134  
STUDY NO: 134  
ABBR: GLU

SEX: MALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	119	107	112	112
8143	113	106	131	117
8148	126	121	115	126
8153	125	114	108	132
MEAN	121	112	117	122
SD	6.0	7.0	10.1	9.0
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	116	108	109	110
8170	120	120	104	117
8147	118	100	112	110
8151	123	128	118	111
MEAN	119	114	111	112
SD	3.0	12.4	5.9	3.4
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	99	95	106	100
8159	99	120	110	113
8175	123	95	115	115
8166	112	108	107	116
MEAN	108	105	110	111
SD	11.6	12.0	4.0	7.4
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	108	93	106	100
8156	129	129	116	118
8160	110	102	111	116
8144	104	99	103	104
MEAN	113	106	109	110
SD	11.1	15.9	5.7	8.9
N	4	4	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Glucose

STUDY ID: 134  
STUDY NO: 134  
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	125	109	111	102
8214	122	101	111	110
8184	127	113	117	115
8180	89	95	89	86
MEAN	116	105	107	103
SD	18.0	8.1	12.3	12.7
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	105	114	106	107
8206	126	104	122	107
8185	124	85	92	102
8199	109	101	104	94
MEAN	116	101	106	103
SD	10.6	12.0	12.3	6.1
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	123	115	125	115
8193	114	114	115	105
8181	115	109	121	111
8197	124	119	117	128
MEAN	119	114	120	115
SD	5.2	4.1	4.4	9.7
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	123	103	125	112
8213	120	133	108	111
8194	106	104	97	107
8182	116	100	106	99
MEAN	116	110	109	107
SD	7.4	15.4	11.7	5.9
N	4	4	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Haptoglobin

STUDY ID: 134  
STUDY NO: 134  
ABBR: HAPT

SEX: MALE

UNITS: mg/dL

ANIMAL ID Week -3 Wk -2/-1 Week 2 Week 5

GROUP: 1-M:0 mg base/kg/day

8172	72.5	78.5	-- B	77.3
8143	85.9	65.7	52.4	25.7
8148	49.0	80.3	69.2	51.5
8153	41.5	45.3	66.5	71.1
MEAN	62.2	67.5	62.7	56.4
SD	20.58	16.13	9.02	23.23
N	4	4	3	4

GROUP: 2-M:0.1 mg base/kg/day

8173	33.4	-- B	43.6	49.3
8170	31.6	61.5	75.6	43.1
8147	63.0	58.4	69.3	-- B
8151	45.8	45.3	-- B	61.9
MEAN	43.5	55.1	62.8	51.4
SD	14.48	8.60	16.95	9.58
N	4	3	3	3

GROUP: 3-M:0.3 mg base/kg/day

8157	75.4	121.3	109.7	140.5
8159	59.5	81.1	87.4	134.2
8175	133.2	107.6	-- B	104.7
8166	56.3	107.3	51.7	80.7
MEAN	81.1	104.3	82.9	115.0
SD	35.72	16.80	29.26	27.70
N	4	4	3	4

GROUP: 4-M:1.0 mg base/kg/day

8146	88.7	103.2	90.8	260.9
8156	62.4	88.0	110.9	254.7
8160	84.9	98.2	98.1	260.3
8144	69.6	96.3	202.5	263.7
MEAN	76.4	96.4	125.6	259.9
SD	12.46	6.33	51.95	3.77
N	4	4	4	4

(--)-Data Unavailable

B - Below Limit of Detection

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

IND. ANIMAL CLINICAL CHEMISTRY REPORT BY GROUP  
TEST: Haptoglobin

STUDY ID: 134  
STUDY NO: 134  
ABBR: HAPT

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	35.9	-- B	-- B	-- B
8214	25.6	-- B	-- B	-- B
8184	59.5	-- B	-- B	106.5
8180	103.4	92.5	76.8	20.4
MEAN	56.1	92.5	76.8	63.5
SD	34.58	NA	NA	60.88
N	4	1	1	2

GROUP: 2-F:0.1 mg base/kg/day				
8207	-- B	-- B	-- B	-- B
8206	37.6	15.8	74.1	17.2
8185	40.0	86.6	68.9	-- B
8199	187.7	95.4	-- B	-- B
MEAN	88.4	65.9	71.5	17.2
SD	85.98	43.64	3.68	NA
N	3	3	2	1

GROUP: 3-F:0.3 mg base/kg/day				
8215	-- B	75.5	35.5	-- B
8193	-- B	-- B	-- B	-- B
8181	-- B	84.4	-- B	-- B
8197	17.1	-- B	-- B	-- B
MEAN	17.1	80.0	35.5	NA
SD	NA	6.29	NA	NA
N	1	2	1	0

GROUP: 4-F:1.0 mg base/kg/day				
8196	56.6	50.4	84.5	218.7
8213	75.0	-- B	35.7	258.4
8194	-- B	-- B	18.8	183.4
8182	25.9	-- B	-- B	150.9
MEAN	52.5	50.4	46.3	202.9
SD	24.81	NA	34.12	46.24
N	3	1	3	4

(--)-Data Unavailable  
B - Below Limit of Detection

NA-Not Applicable

LABCAT CC4.25

**DRAFT**

APPENDIX 7

Individual Hematology Data

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

**DRAFT**

Hematology Test Directory

STUDY: 134

NO.	ABBR. UNITS	DESCRIPTION PRECISION	CALCULATED	OPERAND A	OPERAND B	---LOWER LIMIT---		---UPPER LIMIT---	
						MALE	FEMALE	MALE	FEMALE
1.	RBC 10 <sup>6</sup> /cmm	Erythrocytes 0.00	NO			6.00	6.00	8.00	8.00
2.	HGB g/dL	Hemoglobin 0.0	NO			12.0	12.0	19.0	19.0
3.	HCT %	Hematocrit 0.0	NO			35.0	35.0	55.0	55.0
4.	MCV fL	Mean Corpuscular Volume 0.0	NO			57.0	57.0	70.0	70.0
5.	MCH pg	Mean Corpuscular Hemo. 0.0	NO			20.	20	25	25
6.	MCHC g/dL	Mean Corpus. Hemo. Conc. 0.0	NO			32.0	32.0	38.0	38.0
7.	RETICS %RBCs	Reticulocytes 0.0	NO			0.0	0.0	1.0	1.0
8.	HB %	Heinz Bodies 0.0	NO			0.0	0.0	20.0	20.0
9.	%METHGB %	% Methemoglobin 0.0	NO			0.0	0.0	3.0	3.0
10.	PLT 10 <sup>3</sup> /cmm	Platelets Integer	NO			200	200	500	500
11.	PT sec	Prothrombin Time 0.0	NO			6.0	6.0	9.0	9.0
12.	APTT sec	Act. Partial Thrombo. Time 0.0	NO			7.0	7.0	12.0	12.0
13.	WBC 10 <sup>3</sup> /cmm	Leukocytes 0.0	NO			7.0	7.0	15.0	15.0

(END OF REPORT)

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: RBC

SEX: MALE

UNITS: 10<sup>6</sup>/cmm

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	6.41	6.56	6.57	6.18
8143	6.41	6.48	6.11	6.85
8148	5.38	5.99	5.21	5.99
8153	6.57	6.52	7.06	7.00
MEAN	6.19	6.39	6.24	6.51
SD	0.547	0.267	0.787	0.495
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	6.29	5.80	5.63	5.57
8170	6.02	5.94	6.19	6.29
8147	6.30	6.16	6.80	6.00
8151	5.84	6.80	6.16	5.58
MEAN	6.11	6.18	6.20	5.86
SD	0.223	0.442	0.478	0.350
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	6.23	5.72	6.12	5.52
8159	6.85	6.70	6.41	5.83
8175	6.28	6.19	6.47	6.52
8166	6.11	6.25	6.26	6.18
MEAN	6.37	6.22	6.32	6.01
SD	0.329	0.401	0.157	0.433
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	6.70	6.43	6.44	6.34
8156	6.65	6.58	7.05	6.12
8160	5.45	5.33	5.56	5.02
8144	5.94	5.91	5.91	5.48
MEAN	6.19	6.06	6.24	5.74
SD	0.600	0.566	0.650	0.603
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Erythrocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: RBC

SEX: FEMALE

UNITS:  $10^6/\text{cmm}$

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	6.22	6.19	6.00	6.22
8214	6.05	6.23	6.34	5.91
8184	7.20	6.49	6.42	5.65
8180	6.18	6.36	6.77	6.44
MEAN	6.41	6.32	6.38	6.06
SD	0.530	0.136	0.316	0.347
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	6.35	6.66	7.27	5.75
8206	6.49	5.94	5.69	6.16
8185	7.58	5.77	6.69	6.62
8199	5.78	6.02	6.14	6.44
MEAN	6.55	6.10	6.45	6.24
SD	0.752	0.389	0.684	0.379
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	6.22	6.32	7.02	5.87
8193	6.63	6.11	6.19	5.84
8181	6.62	6.36	6.63	6.06
8197	6.52	6.27	6.32	5.73
MEAN	6.50	6.27	6.54	5.88
SD	0.192	0.110	0.369	0.137
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	6.95	6.56	6.95	5.86
8213	5.95	6.43	5.81	5.06
8194	6.38	6.64	6.61	5.81
8182	6.70	6.65	6.69	5.14
MEAN	6.50	6.57	6.52	5.47
SD	0.432	0.102	0.492	0.426
N	4	4	4	4

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: HemoglobinSTUDY ID: 134  
STUDY NO: 134  
ABBR: HGB

SEX: MALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	15.5	15.7	15.9	14.6
8143	15.5	15.4	14.6	16.3
8148	13.7	15.3	13.6	15.3
8153	15.9	16.0	17.3	17.0
MEAN	15.2	15.6	15.4	15.8
SD	0.98	0.32	1.61	1.06
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	15.6	14.1	13.6	12.6
8170	14.8	14.5	15.1	15.0
8147	15.3	14.9	16.5	14.4
8151	14.0	16.5	14.8	13.4
MEAN	14.9	15.0	15.0	13.9
SD	0.70	1.05	1.19	1.06
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	15.8	14.4	15.7	13.8
8159	16.9	16.5	15.7	14.4
8175	15.5	14.8	15.7	15.8
8166	15.0	15.3	15.5	15.1
MEAN	15.8	15.3	15.7	14.8
SD	0.80	0.91	0.10	0.87
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	16.3	15.6	15.8	15.1
8156	16.2	16.0	17.3	14.9
8160	13.5	13.1	13.9	12.2
8144	14.4	14.5	14.4	13.5
MEAN	15.1	14.8	15.4	13.9
SD	1.38	1.30	1.53	1.35
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hemoglobin

STUDY ID: 134  
STUDY NO: 134  
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	15.0	14.6	14.6	14.7
8214	15.1	15.3	15.6	14.3
8184	18.3	16.4	16.5	14.0
8180	15.3	15.7	16.5	15.5
MEAN	15.9	15.5	15.8	14.6
SD	1.59	0.75	0.91	0.65
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	15.4	16.0	17.8	13.8
8206	15.9	14.2	13.7	14.6
8185	18.9	14.4	17.6	16.2
8199	14.8	15.3	15.4	16.4
MEAN	16.3	15.0	16.1	15.3
SD	1.82	0.83	1.95	1.26
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	15.4	15.7	17.3	14.6
8193	16.4	15.1	15.7	14.9
8181	16.6	15.7	16.3	15.0
8197	16.6	16.2	16.3	14.6
MEAN	16.3	15.7	16.4	14.8
SD	0.57	0.45	0.66	0.21
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	15.6	15.1	16.4	14.5
8213	15.1	16.0	14.6	12.2
8194	15.7	16.2	16.2	14.0
8182	17.0	16.6	16.9	12.8
MEAN	15.9	16.0	16.0	13.4
SD	0.81	0.63	0.99	1.06
N	4	4	4	4

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 134  
STUDY NO: 134  
ABBR: HCT

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	45.4	46.7	46.5	43.3
8143	44.2	44.5	41.8	46.2
8148	39.4	44.0	38.0	44.1
8153	46.0	45.3	49.3	48.3
MEAN	43.8	45.1	43.9	45.5
SD	2.99	1.18	5.00	2.25
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	43.7	40.1	38.6	36.9
8170	42.1	41.0	42.7	43.9
8147	43.7	42.2	46.6	41.3
8151	39.7	46.5	42.3	38.7
MEAN	42.3	42.5	42.6	40.2
SD	1.89	2.83	3.27	3.06
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	45.3	41.2	44.2	40.7
8159	48.3	46.6	44.7	40.9
8175	43.3	42.5	44.3	45.5
8166	43.0	44.2	44.3	44.1
MEAN	45.0	43.6	44.4	42.8
SD	2.44	2.33	0.22	2.38
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	46.4	44.4	44.6	44.4
8156	46.9	46.1	49.7	45.2
8160	39.0	37.6	39.6	37.3
8144	42.1	41.8	41.6	40.5
MEAN	43.6	42.5	43.9	41.9
SD	3.75	3.70	4.39	3.66
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Hematocrit

STUDY ID: 134  
STUDY NO: 134  
ABBR: HCT

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	42.6	42.3	41.1	42.5
8214	43.3	43.8	44.4	41.5
8184	52.4	46.9	46.3	40.1
8180	42.9	44.4	47.5	45.1
MEAN	45.3	44.4	44.8	42.3
SD	4.74	1.92	2.79	2.11
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	44.1	45.6	49.7	39.4
8206	45.1	40.7	39.5	42.8
8185	53.2	40.8	49.8	46.9
8199	41.9	43.3	44.3	46.7
MEAN	46.1	42.6	45.8	44.0
SD	4.93	2.33	4.94	3.57
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	44.3	44.2	49.3	42.6
8193	47.1	43.6	44.8	42.7
8181	46.9	44.8	47.1	43.4
8197	48.8	46.1	46.9	43.8
MEAN	46.8	44.7	47.0	43.1
SD	1.86	1.07	1.84	0.57
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	45.2	43.0	46.7	43.9
8213	42.9	45.7	41.4	38.0
8194	43.6	45.0	44.8	40.2
8182	47.5	46.9	47.4	37.7
MEAN	44.8	45.2	45.1	40.0
SD	2.04	1.63	2.68	2.86
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Volume

STUDY ID: 134  
STUDY NO: 134  
ABBR: MCV

SEX: MALE

UNITS: fL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	70.8	71.2	70.8	70.1
8143	69.0	68.7	68.4	67.4
8148	73.2	73.5	72.9	73.6
8153	70.0	69.5	69.8	69.0
MEAN	70.8	70.7	70.5	70.0
SD	1.79	2.12	1.89	2.63
N	4	4	4	4

GROUP: 2-M:D.1 mg base/kg/day				
8173	69.5	69.1	68.6	66.2
8170	69.9	69.0	69.0	69.8
8147	69.4	68.5	68.5	68.8
8151	68.0	68.4	68.7	69.4
MEAN	69.2	68.8	68.7	68.6
SD	0.83	0.35	0.22	1.62
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	72.7	72.0	72.2	73.7
8159	70.5	69.6	69.7	70.2
8175	68.9	68.7	68.5	69.8
8166	70.4	70.7	70.8	71.4
MEAN	70.6	70.3	70.3	71.3
SD	1.56	1.42	1.58	1.75
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	69.3	69.1	69.3	70.0
8156	70.5	70.1	70.5	73.9
8160	71.6	70.5	71.2	74.3
8144	70.9	70.7	70.4	73.9
MEAN	70.6	70.1	70.4	73.0
SD	0.96	0.71	0.79	2.03
N	4	4	4	4

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular VolumeSTUDY ID: 134  
STUDY NO: 134  
ABBR: MCV

SEX: FEMALE

UNITS: fL

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	68.5	68.3	68.5	68.3
8214	71.6	70.3	70.0	70.2
8184	72.8	72.3	72.1	71.0
8180	69.4	69.8	70.2	70.0
MEAN	70.6	70.2	70.2	69.9
SD	1.97	1.65	1.48	1.14
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	69.4	68.5	68.4	68.5
8206	69.5	68.5	69.4	69.5
8185	70.2	70.7	71.2	70.8
8199	72.5	71.9	72.1	72.5
MEAN	70.4	69.9	70.3	70.3
SD	1.44	1.69	1.68	1.73
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	71.2	69.9	70.2	72.6
8193	71.0	71.4	72.4	73.1
8181	70.8	70.4	71.0	71.6
8197	74.8	73.5	74.2	76.4
MEAN	72.0	71.3	72.0	73.4
SD	1.91	1.59	1.75	2.08
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	65.0	65.5	67.2	74.9
8213	72.1	71.1	71.3	75.1
8194	68.3	67.8	67.8	69.2
8182	70.9	70.5	70.9	73.3
MEAN	69.1	68.7	69.3	73.1
SD	3.15	2.59	2.10	2.74
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Hemo.

STUDY ID: 134  
STUDY NO: 134  
ABBR: MCH

SEX: MALE

UNITS: pg

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	24.2	23.9	24.2	23.6
8143	24.2	23.8	23.9	23.8
8148	25.5	25.5	26.1	25.5
8153	24.2	24.5	24.5	24.3
MEAN	24.5	24.4	24.7	24.3
SD	0.65	0.78	0.98	0.85
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	24.8	24.3	24.2	22.6
8170	24.6	24.4	24.4	23.8
8147	24.3	24.2	24.3	24.0
8151	24.0	24.3	24.0	24.0
MEAN	24.4	24.3	24.2	23.6
SD	0.35	0.08	0.17	0.67
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	25.4	25.2	25.7	25.0
8159	24.7	24.6	24.5	24.7
8175	24.7	23.9	24.3	24.2
8166	24.5	24.5	24.8	24.4
MEAN	24.8	24.6	24.8	24.6
SD	0.39	0.53	0.62	0.35
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	24.3	24.3	24.5	23.8
8156	24.4	24.3	24.5	24.3
8160	24.8	24.6	25.0	24.3
8144	24.2	24.5	24.4	24.6
MEAN	24.4	24.4	24.6	24.3
SD	0.26	0.15	0.27	0.33
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpuscular Hemo.

STUDY ID: 134  
STUDY NO: 134  
ABBR: MCH

SEX: FEMALE

UNITS: pg

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	24.1	23.6	24.3	23.6
8214	25.0	24.6	24.6	24.2
8184	25.4	25.3	25.7	24.8
8180	24.8	24.7	24.4	24.1
MEAN	24.8	24.6	24.8	24.2
SD	0.54	0.70	0.65	0.49
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	24.3	24.0	24.5	24.0
8206	24.5	23.9	24.1	23.7
8185	24.9	25.0	25.2	24.5
8199	25.6	25.4	25.1	25.5
MEAN	24.8	24.6	24.7	24.4
SD	0.57	0.74	0.52	0.79
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	24.8	24.8	24.6	24.9
8193	24.7	24.7	25.4	25.5
8181	25.1	24.7	24.6	24.8
8197	25.5	25.8	25.8	25.5
MEAN	25.0	25.0	25.1	25.2
SD	0.36	0.54	0.60	0.38
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	22.4	23.0	23.6	24.7
8213	25.4	24.9	25.1	24.1
8194	24.6	24.4	24.5	24.1
8182	25.4	25.0	25.3	24.9
MEAN	24.5	24.3	24.6	24.5
SD	1.42	0.92	0.76	0.41
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: 134  
STUDY NO: 134  
ABBR: MCHC

SEX: MALE

UNITS: g/dl

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	34.1	33.6	34.2	33.7
8143	35.1	34.6	34.9	35.3
8148	34.8	34.8	35.8	34.7
8153	34.6	35.3	35.1	35.2
MEAN	34.7	34.6	35.0	34.7
SD	0.42	0.71	0.66	0.73
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	35.7	35.2	35.2	34.1
8170	35.2	35.4	35.4	34.2
8147	35.0	35.3	35.4	34.9
8151	35.3	35.5	35.0	34.6
MEAN	35.3	35.4	35.3	34.5
SD	0.29	0.13	0.19	0.37
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	34.9	35.0	35.5	33.9
8159	35.0	35.4	35.1	35.2
8175	35.8	34.8	35.4	34.7
8166	34.9	34.6	35.0	34.2
MEAN	35.2	35.0	35.3	34.5
SD	0.44	0.34	0.24	0.57
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	35.1	35.1	35.4	34.0
8156	34.5	34.7	34.8	33.0
8160	34.6	34.8	35.1	32.7
8144	34.2	34.7	34.6	33.3
MEAN	34.6	34.8	35.0	33.3
SD	0.37	0.19	0.35	0.56
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: 134  
STUDY NO: 134  
ABBR: MCHC

SEX: FEMALE

UNITS: g/dl

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	35.2	34.5	35.5	34.6
8214	34.9	34.9	35.1	34.5
8184	34.9	35.0	35.6	34.9
8180	35.7	35.4	34.7	34.4
MEAN	35.2	35.0	35.2	34.6
SD	0.38	0.37	0.41	0.22
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	34.9	35.1	35.8	35.0
8206	35.3	34.9	34.7	34.1
8185	35.5	35.3	35.3	34.5
8199	35.3	35.3	34.8	35.1
MEAN	35.3	35.2	35.2	34.7
SD	0.25	0.19	0.51	0.46
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	34.8	35.5	35.1	34.3
8193	34.8	34.6	35.0	34.9
8181	35.4	35.0	34.6	34.6
8197	34.0	35.1	34.8	33.3
MEAN	34.8	35.1	34.9	34.3
SD	0.57	0.37	0.22	0.69
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	34.5	35.1	35.1	33.0
8213	35.2	35.0	35.3	32.1
8194	36.0	36.0	36.2	34.8
8182	35.8	35.4	35.7	34.0
MEAN	35.4	35.4	35.6	33.5
SD	0.68	0.45	0.49	1.18
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: RETICS

SEX: MALE

UNITS: %RBCs

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.2	0.1	0.0	0.0
8143	0.4	0.5	0.5	0.4
8148	0.1	0.2	0.0	0.2
8153	0.4	0.1	0.3	0.2
MEAN	0.3	0.2	0.2	0.2
SD	0.15	0.19	0.24	0.16
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	0.3	0.1	0.1	0.1
8170	0.1	0.0	0.0	0.2
8147	0.2	0.1	0.2	0.2
8151	0.1	0.1	0.2	0.2
MEAN	0.2	0.1	0.1	0.2
SD	0.10	0.05	0.10	0.05
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	0.6	0.7	0.8	0.9
8159	0.3	0.5	0.2	0.4
8175	0.2	0.2	0.5	0.7
8166	0.3	0.3	0.4	0.1
MEAN	0.4	0.4	0.5	0.5
SD	0.17	0.22	0.25	0.35
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	0.1	0.0	0.1	0.6
8156	0.2	0.7	0.3	0.9
8160	0.4	0.2	0.6	1.6
8144	0.5	0.4	0.6	1.4
MEAN	0.3	0.3	0.4	1.1
SD	0.18	0.30	0.24	0.46
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Reticulocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: RETICS

SEX: FEMALE

UNITS: %RBCs

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.2	0.2	0.4	0.0
8214	0.4	0.2	0.5	0.6
8184	0.6	0.2	0.1	0.1
8180	0.0	0.1	0.1	0.1
MEAN	0.3	0.2	0.3	0.2
SD	0.26	0.05	0.21	0.27
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.0	0.2	0.2	0.2
8206	0.2	0.0	0.3	0.3
8185	1.0	0.2	0.8	0.7
8199	0.0	0.3	0.5	0.2
MEAN	0.3	0.2	0.5	0.4
SD	0.48	0.13	0.26	0.24
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.0	0.2	0.4	0.4
8193	0.7	0.4	0.5	0.7
8181	0.2	0.2	0.2	0.4
8197	0.5	0.6	0.6	0.5
MEAN	0.4	0.4	0.4	0.5
SD	0.31	0.19	0.17	0.14
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.2	0.2	0.6	1.0
8213	0.3	0.4	0.8	0.9
8194	0.2	0.5	0.9	1.7
8182	0.3	0.4	1.0	0.7
MEAN	0.3	0.4	0.8	1.1
SD	0.06	0.13	0.17	0.43
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 134  
STUDY NO: 134  
ABBR: NRBC

SEX: MALE

UNITS: #/100 WBC

Animal ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0	0	0	0
8143	0	0	0	0
8148	0	0	0	0
8153	0	0	0	0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

Animal ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	0	0	0	0
8170	0	0	0	0
8147	0	0	0	0
8151	0	0	0	0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

Animal ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	0	0	0	0
8159	0	0	0	0
8175	0	0	0	0
8166	0	0	0	0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

Animal ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	0	0	0	0
8156	0	0	0	0
8160	0	0	0	1
8144	0	0	0	0
MEAN	0.0	0.0	0.0	0.3
SD	0.00	0.00	0.00	0.50
N	4	4	4	4

WBC corrected for NRBC = or > 10

LABCAT HE4.3

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Nucleated Red Cells

STUDY ID: 134  
STUDY NO: 134  
ABBR: NRBC

SEX: FEMALE

UNITS: #/100 WBC

Animal ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0	0	0	0
8214	0	0	0	0
8184	0	0	0	0
8180	0	0	0	0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0	0	0	0
8206	0	0	0	0
8185	0	0	0	1
8199	0	0	0	0
MEAN	0.0	0.0	0.0	0.3
SD	0.00	0.00	0.00	0.50
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0	0	0	0
8193	0	0	0	0
8181	0	0	0	0
8197	0	0	0	0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0	0	0	1
8213	0	0	0	5
8194	0	0	1	0
8182	0	0	4	0
MEAN	0.0	0.0	1.3	1.5
SD	0.00	0.00	1.89	2.38
N	4	4	4	4

WBC corrected for NRBC = or > 10

LABCAT HE4.3

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 134  
STUDY NO: 134  
ABBR: HB

SEX: MALE

UNITS: %

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.0	0.0	0.0	0.0
8143	0.0	0.0	0.1	0.3
8148	0.0	0.0	0.2	0.0
8153	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.1	0.1
SD	0.00	0.00	0.10	0.15
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	0.0	0.0	0.0	0.0
8170	0.0	0.2	0.0	0.4
8147	0.0	0.0	0.0	0.2
8151	0.0	0.0	0.0	0.0
MEAN	0.0	0.1	0.0	0.2
SD	0.00	0.10	0.00	0.19
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	0.1	0.0	0.0	0.1
8159	0.0	0.3	0.0	0.2
8175	0.0	0.1	0.2	0.0
8166	0.0	0.0	0.0	0.0
MEAN	0.0	0.1	0.1	0.1
SD	0.05	0.14	0.10	0.10
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	0.0	0.0	0.0	0.0
8156	0.0	0.0	0.1	0.1
8160	0.0	0.0	0.3	0.6
8144	0.0	0.0	0.2	0.0
MEAN	0.0	0.0	0.2	0.2
SD	0.00	0.00	0.13	0.29
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Heinz Bodies

STUDY ID: 134  
STUDY NO: 134  
ABBR: HB

SEX: FEMALE

UNITS: %

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.0	0.0	0.2	0.0
8214	0.0	0.0	0.1	0.0
8184	0.0	0.0	0.0	0.0
8180	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.1	0.0
SD	0.00	0.00	0.10	0.00
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-F:0.1 mg base/kg/day				
8207	0.0	0.0	0.0	0.0
8206	0.0	0.0	0.3	0.0
8185	0.0	0.0	0.2	0.0
8199	0.0	0.0	0.1	0.0
MEAN	0.0	0.0	0.2	0.0
SD	0.00	0.00	0.13	0.00
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-F:0.3 mg base/kg/day				
8215	0.1	0.0	0.1	0.3
8193	0.0	0.0	0.3	0.0
8181	0.0	0.0	0.0	0.0
8197	0.0	0.0	0.3	0.0
MEAN	0.0	0.0	0.2	0.1
SD	0.05	0.00	0.15	0.15
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-F:1.0 mg base/kg/day				
8196	0.0	0.0	0.0	0.0
8213	0.1	0.4	0.8	0.0
8194	0.1	0.0	0.0	0.3
8182	0.0	0.0	0.3	0.5
MEAN	0.1	0.1	0.3	0.2
SD	0.06	0.20	0.38	0.24
N	4	4	4	4

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % MethemoglobinSTUDY ID: 134  
STUDY NO: 134  
ABBR: %METHGB

SEX: MALE

UNITS: %

Animal ID	Week -3	Wk -2/-1	Day 0	Week 2	Week 3	Week 4	Week 5
GROUP: 1-M:0 mg base/kg/day							
8172	1.0	0.7	0.8	1.1	0.8	0.7	1.1
8143	1.4	1.2	1.0	1.7	2.0	1.7	2.3
8148	0.8	0.9	0.8	1.0	1.1	1.0	0.8
8153	1.0	1.0	0.9	1.2	1.2	0.7	0.8
MEAN	1.1	1.0	0.9	1.3	1.3	1.0	1.3
SD	0.25	0.21	0.10	0.31	0.51	0.47	0.71
N	4	4	4	4	4	4	4
GROUP: 2-M:0.1 mg base/kg/day							
8173	0.9	0.7	0.7	1.3	1.8	2.0	1.8
8170	1.1	1.2	1.3	2.0	3.6	3.8	3.5
8147	1.0	0.8	0.8	1.1	1.2	1.4	1.7
8151	0.8	0.8	0.8	1.1	2.8	3.0	2.4
MEAN	1.0	0.9	0.9	1.4	2.4	2.6	2.4
SD	0.13	0.22	0.27	0.43	1.06	1.06	0.83
N	4	4	4	4	4	4	4
GROUP: 3-M:0.3 mg base/kg/day							
8157	1.3	0.9	0.9	6.9	10.0	9.9	9.7
8159	0.8	0.9	1.0	2.1	6.6	6.3	5.8
8175	1.1	1.1	1.0	8.3	8.9	8.2	7.5
8166	0.8	0.8	1.2	7.4	8.9	9.7	9.4
MEAN	1.0	0.9	1.0	6.2	8.6	8.5	8.1
SD	0.24	0.13	0.13	2.78	1.43	1.67	1.82
N	4	4	4	4	4	4	4
GROUP: 4-M:1.0 mg base/kg/day							
8146	1.0	1.3	0.8	26.0	27.5	28.2	24.6
8156	0.8	0.9	1.0	20.5	25.2	24.5	21.5
8160	1.1	1.0	1.1	22.2	24.5	24.7	27.9
8144	0.9	0.9	1.1	30.0	31.6	28.8	28.7
MEAN	1.0	1.0	1.0	24.7	27.2	26.6	25.7
SD	0.13	0.19	0.14	4.23	3.20	2.27	3.30
N	4	4	4	4	4	4	4

LABCAT HE4.3

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: % Methemoglobin

STUDY IO: 134  
STUDY NO: 134  
ABBR: %METHGB

SEX: FEMALE

UNITS: %

Animal IO	Week -3	Wk -2/-1	Day 0	Week 2	Week 3	Week 4	Week 5
GROUP: 1-F:0 mg base/kg/day							
8211	0.8	1.0	0.8	1.0	1.0	0.8	1.2
8214	0.7	0.6	0.8	0.6	0.8	0.6	0.9
8184	1.2	0.8	1.1	0.9	1.2	1.5	1.4
8180	0.7	0.8	1.0	0.8	0.9	0.7	0.8
MEAN	0.9	0.8	0.9	0.8	1.0	0.9	1.1
SD	0.24	0.16	0.15	0.17	0.17	0.41	0.28
N	4	4	4	4	4	4	4
GROUP: 2-F:0.1 mg base/kg/day							
8207	0.8	0.6	0.6	1.2	1.6	1.9	2.2
8206	0.6	0.7	0.7	1.2	1.6	1.8	2.3
8185	2.3	1.3	0.7	2.8	2.7	2.8	2.2
8199	0.9	0.8	0.9	2.3	2.7	2.7	2.5
MEAN	1.2	0.9	0.7	1.9	2.2	2.3	2.3
SD	0.78	0.31	0.13	0.81	0.64	0.52	0.14
N	4	4	4	4	4	4	4
GROUP: 3-F:0.3 mg base/kg/day							
8215	0.7	0.7	0.8	9.3	11.0	9.5	7.2
8193	0.6	0.7	1.1	6.0	9.3	9.7	8.8
8181	0.8	0.8	0.6	3.4	6.4	6.3	6.7
8197	1.1	1.2	0.9	11.0	13.3	11.6	9.3
MEAN	0.8	0.9	0.9	7.4	10.0	9.3	8.0
SD	0.22	0.24	0.21	3.39	2.91	2.20	1.25
N	4	4	4	4	4	4	4
GROUP: 4-F:1.0 mg base/kg/day							
8196	0.8	1.1	0.7	15.6	20.2	17.9	15.6
8213	0.8	0.7	1.0	37.0	37.8	32.5	30.1
8194	0.9	0.9	0.8	24.6	28.9	24.7	22.0
8182	0.7	0.8	1.2	30.2	30.5	26.0	26.4
MEAN	0.8	0.9	0.9	26.9	29.4	25.3	23.5
SD	0.08	0.17	0.22	9.05	7.23	5.98	6.24
N	4	4	4	4	4	4	4

LABCAT HE4.3

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8172	Poikilocytes,Slight	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells
8143	Polychromasia,Slight	Normal Red Blood Cells	Polychromasia,Slight Macrocytes,Slight; Clumped Platelets, Moderate	Normal Red Blood Cells
8148	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis, Moderate;Macrocytes, Moderate;;Decreased Platelets,Slight	Normal Red Blood Cells;Clumped Platelets,Slight
8153	Polychromasia,Slight	Polychromasia, Moderate; Anisocytosis, Moderate	Polychromasia,Slight Anisocytosis,Slight	Normal Red Blood Cells

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8173	Normal Red Blood Cells; Clumped Platelets, Slight	Normal Red Blood Cells	Poikilocytes, Slight; Target Cells, Slight; Clumped Platelets, Moderate	Normal Red Blood Cells; Decreased Platelets, Slight
8170	Poikilocytes, Moderate	Poikilocytes, Moderate; Anisocytosis, Moderate; Macrocytes, Moderate	Normal Red Blood Cells	Polychromasia, Slight; Poikilocytes, Slight; Anisocytosis, Moderate
8147	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Polychromasia, Slight; Macrocytes, Slight
8151	Normal Red Blood Cells	Poikilocytes, Moderate; Anisocytosis, Slight	Normal Red Blood Cells	Normal Red Blood Cells

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8157	Polychromasia,Slight Macrocytes,Slight	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight; Clumped Platelets, Moderate	Polychromasia, Moderate; Anisocytosis,Slight; Decreased Platelets, Moderate
8159	Anisocytosis,Slight	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis, Moderate	Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate; Clumped Platelets, Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis,Mod. to Marked;Decreased Platelets,Mod. to Marked
8175	Normal Red Blood Cells	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia, Moderate;Macrocytes, Moderate;Clumped Platelets,Slight	Anisocytosis, Moderate;Decreased Platelets,Moderate
8166	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight	Poikilocytes,Slight; Anisocytosis,Slight; Macrocytes,Slight; Clumped Platelets, Slight	Anisocytosis, Moderate;Decreased Platelets,Moderate

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8146	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis,Slight; Decreased Platelets, Moderate	Polychromasia,Slight Poikilocytes,Slight; Decreased Platelets, Slight
8156	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis, Moderate;Macrocytes, Moderate	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Slight;; Decreased Platelets, Mod. to Marked	Polychromasia,Slight Poikilocytes, Moderate;Decreased Platelets,Moderate
8160	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis, Moderate;Macrocytes, Moderate	Polychromasia,Slight Macrocytes,Slight; Large Platelets, Slight;Decreased Platelets,Slight	Polychromasia, Moderate;Macrocytes, Moderate;Clumped Platelets,Mod. to Marked
8144	Normal Red Blood Cells	Normal Red Blood Cells	Anisocytosis, Moderate;Clumped Platelets,Mod. to Marked	Polychromasia,Slight Macrocytes,Slight; Clumped Platelets, Slight

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8211	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate; Anisocytosis, Moderate	Polychromasia,Slight Macrocytes,Slight	Normal Red Blood Cells
8214	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells	Polychromasia,Slight Macrocytes,Slight	Normal Red Blood Cells
8184	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells	Normal Red Blood Cells
8180	Poikilocytes,Slight; Clumped Platelets, Slight	Anisocytosis,Slight	Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight; Decreased Platelets, Slight

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8207	Poikilocytes, Moderate; Anisocytosis,Slight	Anisocytosis,Slight; Macrocytes,Slight	Polychromasia,Slight Poikilocytes,Slight	Poikilocytes,Slight; Anisocytosis,Slight; Decreased Platelets, Slight
8206	Polychromasia,Slight Poikilocytes, Moderate	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight; Macrocytes,Slight; Clumped Platelets, Slight	Poikilocytes,Slight; Anisocytosis,Slight
8185	Polychromasia, Moderate;Macrocytes, Moderate	Anisocytosis,Slight; Macrocytes,Slight	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis, Moderate;Clumped Platelets,Slight	Normal Red Blood Cells
8199	Anisocytosis, Moderate;Macrocytes, Moderate	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight	Normal Red Blood Cells

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

## RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134  
STUDY NO: 134

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
8215	Normal Red Blood Cells	Poikilocytes,Slight; Anisocytosis,Slight	Anisocytosis, Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis, Moderate;Decreased Platelets,Slight
8193	Poikilocytes,Slight; Clumped Platelets, Mod. to Marked	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight; Decreased Platelets, Moderate	Polychromasia,Slight Macrocytes,Slight; Decreased Platelets, Mod. to Marked
8181	Anisocytosis,Slight; Poikilocytes,Slight	Anisocytosis, Moderate;Macrocytes, Moderate	Poikilocytes,Slight; Anisocytosis,Slight	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Slight; Clumped Platelets, Mod. to Marked
8197	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate;Macrocytes, Moderate	Normal Red Blood Cells; Clumped Platelets, Moderate

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

RBC MORPHOLOGY OBSERVATIONS

STUDY ID: 134 STUDY NO: 134		GROUP: 4-F : 1.0 mg base/kg/day			SEX: FEMALE
ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5	
8196	Polychromasia,Slight Anisocytosis,Slight	Anisocytosis,Slight	Polychromasia,Slight Anisocytosis,Slight; Clumped Platelets, Moderate	Polychromasia,Slight Poikilocytes,Slight; Rouleaux Formation, Mod. to Marked; Decreased Platelets, Moderate	
8213	Normal Red Blood Cells	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis, Moderate;Macrocytes, Moderate;Clumped Platelets,Moderate	Polychromasia,Slight Poikilocytes,Mod. to Marked;Anisocytosis, Slight;Clumped Platelets,Mod. to Marked;Decreased Platelets,Mod. to Marked	
8194	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight; Clumped Platelets, Slight	Polychromasia, Moderate; Poikilocytes,Slight; Macrocytes,Moderate; Decreased Platelets, Moderate	
8182	Normal Red Blood Cells	Polychromasia,Slight Macrocytes,Slight	Polychromasia, Moderate; Poikilocytes, Moderate;Macrocytes, Moderate;Clumped Platelets,Slight	Polychromasia,Slight Anisocytosis, Moderate;Decreased Platelets,Moderate	

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: WBC

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	4.9	5.3	5.0	6.1
8143	9.8	9.2	9.6	9.2
8148	7.3	7.7	7.5	7.4
8153	5.9	10.0	7.2	11.2
MEAN	7.0	8.1	7.3	8.5
SD	2.13	2.07	1.88	2.22
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	6.1	7.2	6.4	7.5
8170	5.2	5.9	8.9	6.0
8147	7.6	10.2	8.9	6.1
8151	8.2	9.4	8.8	9.9
MEAN	6.8	8.2	8.3	7.4
SD	1.37	1.98	1.23	1.82
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	10.5	18.1	9.4	9.2
8159	8.9	7.8	7.6	8.7
8175	8.5	9.8	10.0	10.4
8166	8.9	9.8	8.6	7.5
MEAN	9.2	11.4	8.9	9.0
SD	0.89	4.58	1.04	1.20
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	7.5	8.6	6.7	7.8
8156	7.6	9.1	5.9	8.8
8160	8.5	9.0	9.5	11.0
8144	8.7	6.6	11.1	8.8
MEAN	8.1	8.3	8.3	9.1
SD	0.61	1.17	2.42	1.35
N	4	4	4	4

WBC corrected for NRBC = or > 10

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DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Leukocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: WBC

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	8.2	7.3	7.5	7.6
8214	7.7	7.9	7.8	9.6
8184	10.8	10.2	9.2	9.6
8180	13.4	10.4	10.6	7.1
MEAN	10.0	9.0	8.8	8.5
SD	2.63	1.58	1.42	1.31
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-F:0.1 mg base/kg/day				
8207	9.3	10.4	12.9	9.0
8206	9.6	9.1	11.8	6.9
8185	8.1	15.6	10.2	6.9
8199	9.1	7.7	7.9	6.4
MEAN	9.0	10.7	10.7	7.3
SD	0.65	3.45	2.17	1.16
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-F:0.3 mg base/kg/day				
8215	7.1	8.2	9.9	7.6
8193	9.3	8.7	8.1	10.1
8181	7.1	12.0	8.7	7.6
8197	7.2	10.8	9.3	7.0
MEAN	7.7	9.9	9.0	8.1
SD	1.08	1.78	0.77	1.38
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-F:1.0 mg base/kg/day				
8196	9.2	8.4	9.1	7.5
8213	7.1	7.0	8.1	6.7
8194	14.2	10.8	9.4	9.2
8182	7.6	9.4	14.8	9.3
MEAN	9.5	8.9	10.4	8.2
SD	3.24	1.60	3.02	1.28
N	4	4	4	4

WBC corrected for NRBC = or &gt; 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. NeutrophilsSTUDY ID: 134  
STUDY NO: 134  
ABBR: M. Neutrop

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
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GROUP: 1-M:0 mg base/kg/day

8172	2.6	3.3	2.5	4.4
8143	5.6	4.4	4.3	6.0
8148	4.6	4.9	5.3	4.1
8153	3.0	6.1	3.7	8.4

MEAN	4.0	4.7	4.0	5.7
SD	1.40	1.16	1.17	1.97
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	3.2	5.0	4.0	4.7
8170	3.1	3.2	6.0	3.0
8147	4.6	7.2	5.1	3.7
8151	4.6	6.3	4.9	5.8

MEAN	3.9	5.4	5.0	4.3
SD	0.84	1.74	0.82	1.22
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	5.6	12.1	4.3	4.4
8159	6.3	5.0	5.5	6.2
8175	6.0	6.0	7.2	8.0
8166	5.5	7.3	6.6	5.3

MEAN	5.9	7.6	5.9	6.0
SD	0.37	3.14	1.28	1.54
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	5.0	6.2	3.8	5.1
8156	4.6	6.2	2.8	5.9
8160	6.5	5.5	6.7	8.0
8144	6.1	4.4	6.8	6.2

MEAN	5.6	5.6	5.0	6.3
SD	0.90	0.85	2.03	1.22
N	4	4	4	4

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: M. Neutrophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: M. Neutrop

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	5.9	4.5	4.7	5.0
8214	4.7	5.1	5.5	6.5
8184	6.3	6.5	6.8	7.1
8180	9.1	6.2	6.8	3.7
MEAN	6.5	5.6	6.0	5.6
SD	1.86	0.94	1.03	1.53
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	6.0	6.1	8.4	6.4
8206	6.4	6.5	8.9	4.8
8185	5.5	12.2	7.5	3.9
8199	6.8	5.1	5.7	4.4
MEAN	6.2	7.5	7.6	4.9
SD	0.56	3.20	1.41	1.08
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	3.6	5.2	6.5	3.6
8193	5.6	5.4	--	6.0
8181	4.0	8.8	6.3	4.2
8197	4.6	6.7	6.9	5.2
MEAN	4.5	6.5	6.6	4.8
SD	0.87	1.66	0.31	1.06
N	4	4	3	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	4.8	4.1	5.5	3.5
8213	4.4	4.0	5.2	3.7
8194	9.2	6.8	6.5	6.3
8182	4.9	6.0	11.2	6.2
MEAN	5.8	5.2	7.1	4.9
SD	2.26	1.40	2.79	1.53
N	4	4	4	4

(---)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. Neutrophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: I. Neutrop

SEX: MALE

UNITS:  $10^3/\text{cmm}$

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.2	0.2	0.1	0.1
8143	0.4	0.2	0.2	0.2
8148	0.2	0.2	0.2	0.1
8153	0.4	0.3	0.1	0.0
MEAN	0.3	0.2	0.2	0.1
SD	0.12	0.05	0.06	0.08
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	0.4	0.4	0.2	0.1
8170	0.2	0.4	0.0	0.3
8147	0.3	0.3	0.2	0.2
8151	0.2	0.2	0.1	0.2
MEAN	0.3	0.3	0.1	0.2
SD	0.10	0.10	0.10	0.08
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	0.7	0.2	0.1	0.1
8159	1.0	0.5	0.3	0.5
8175	0.6	0.5	0.1	0.3
8166	0.5	0.2	0.2	0.2
MEAN	0.7	0.4	0.2	0.3
SD	0.22	0.17	0.10	0.17
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	0.4	0.1	0.2	0.2
8156	0.4	0.5	0.2	0.4
8160	0.2	0.2	0.2	0.3
8144	0.7	0.2	0.4	0.3
MEAN	0.4	0.3	0.3	0.3
SD	0.21	0.17	0.10	0.08
N	4	4	4	4

WBC corrected for NRBC = or > 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: I. NeutrophilsSTUDY ID: 134  
STUDY NO: 134  
ABBR: I. Neutrop

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.2	0.2	0.2	0.3
8214	0.1	0.4	0.1	0.4
8184	0.0	0.1	0.1	0.3
8180	0.5	0.1	0.1	0.1
MEAN	0.2	0.2	0.1	0.3
SD	0.22	0.14	0.05	0.13
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-F:0.1 mg base/kg/day				
8207	0.6	0.1	0.5	0.2
8206	0.1	0.0	0.5	0.0
8185	0.2	0.2	0.3	0.1
8199	0.1	0.0	0.1	0.1
MEAN	0.3	0.1	0.4	0.1
SD	0.24	0.10	0.19	0.08
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-F:0.3 mg base/kg/day				
8215	0.4	0.2	0.0	0.0
8193	0.1	0.2	--	0.1
8181	0.1	0.0	0.1	0.0
8197	0.1	0.5	0.3	0.0
MEAN	0.2	0.2	0.1	0.0
SD	0.15	0.21	0.15	0.05
N	4	4	3	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-F:1.0 mg base/kg/day				
8196	0.2	0.3	0.2	0.0
8213	0.4	0.4	0.3	0.5
8194	0.4	0.0	0.1	0.4
8182	0.1	0.2	0.6	0.1
MEAN	0.3	0.2	0.3	0.3
SD	0.15	0.17	0.22	0.24
N	4	4	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or &gt; 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Lymphocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: Lymphocyte

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	1.7	1.3	2.1	1.3
8143	3.5	4.0	4.0	3.0
8148	2.3	2.1	1.4	2.5
8153	2.3	2.9	3.0	1.8
MEAN	2.5	2.6	2.6	2.2
SD	0.75	1.15	1.13	0.75
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	1.9	1.6	2.0	2.0
8170	1.5	2.2	2.0	2.4
8147	2.0	1.6	3.4	1.5
8151	2.5	2.4	3.2	3.2
MEAN	2.0	2.0	2.7	2.3
SD	0.41	0.41	0.75	0.72
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	3.3	3.1	3.7	3.0
8159	1.2	2.0	1.7	1.0
8175	1.0	2.4	2.2	1.1
8166	2.0	1.6	1.2	1.3
MEAN	1.9	2.3	2.2	1.6
SD	1.04	0.64	1.08	0.94
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	1.7	0.9	1.9	0.8
8156	1.7	2.1	1.9	1.9
8160	1.4	1.9	1.9	1.8
8144	1.6	2.0	2.0	1.2
MEAN	1.6	1.7	1.9	1.4
SD	0.14	0.56	0.05	0.52
N	4	4	4	4

WBC corrected for NRBC = or > 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: LymphocytesSTUDY ID: 134  
STUDY NO: 134  
ABBR: Lymphocyte

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	1.7	2.2	2.2	1.7
8214	1.7	1.8	1.3	2.1
8184	3.9	2.6	1.7	1.7
8180	3.1	2.7	3.2	2.1
MEAN	2.6	2.3	2.1	1.9
SD	1.09	0.41	0.82	0.23
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	2.4	3.5	3.7	2.2
8206	2.7	2.0	1.9	1.9
8185	1.9	2.8	1.2	1.9
8199	1.1	1.7	1.7	1.3
MEAN	2.0	2.5	2.1	1.8
SD	0.70	0.81	1.09	0.38
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	2.4	2.5	2.4	3.3
8193	2.8	2.6	--	3.2
8181	2.5	2.9	2.2	2.7
8197	2.0	2.5	1.1	1.1
MEAN	2.4	2.6	1.9	2.6
SD	0.33	0.19	0.70	1.02
N	4	4	3	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	3.8	3.3	2.0	2.8
8213	2.1	2.3	2.3	1.5
8194	4.1	3.1	1.6	2.0
8182	2.2	2.4	2.4	1.0
MEAN	3.1	2.8	2.1	1.8
SD	1.05	0.50	0.36	0.77
N	4	4	4	4

(--)Data Unavailable

WBC corrected for NRBC = or &gt; 10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: MonocytesSTUDY ID: 134  
STUDY NO: 134  
ABBR: Monocytes

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.1	0.3	0.2	0.1
8143	0.1	0.2	0.4	0.0
8148	0.1	0.1	0.1	0.1
8153	0.1	0.4	0.3	0.8
MEAN	0.1	0.3	0.3	0.3
SD	0.00	0.13	0.13	0.37
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	0.4	0.1	0.1	0.1
8170	0.1	0.0	0.5	0.1
8147	0.2	0.7	0.0	0.1
8151	0.7	0.2	0.2	0.5
MEAN	0.4	0.3	0.2	0.2
SD	0.26	0.31	0.22	0.20
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	0.2	2.0	0.5	0.7
8159	0.2	0.1	0.1	0.8
8175	0.8	0.6	0.4	0.9
8166	0.4	0.4	0.2	0.4
MEAN	0.4	0.8	0.3	0.7
SD	0.28	0.84	0.18	0.22
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	0.3	0.9	0.7	0.9
8156	0.8	0.1	0.9	0.4
8160	0.2	1.0	0.4	0.9
8144	0.1	0.0	1.1	0.4
MEAN	0.4	0.5	0.8	0.7
SD	0.31	0.52	0.30	0.29
N	4	4	4	4

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: MonocytesSTUDY ID: 134  
STUDY NO: 134  
ABBR: Monocytes

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.3	0.2	0.2	0.4
8214	1.0	0.3	0.5	0.4
8184	0.2	0.6	0.2	0.1
8180	0.4	0.6	0.2	0.4
MEAN	0.5	0.4	0.3	0.3
SD	0.36	0.21	0.15	0.15
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.3	0.4	0.3	0.1
8206	0.2	0.3	0.4	0.1
8185	0.3	0.3	0.4	0.5
8199	1.1	0.7	0.1	0.3
MEAN	0.5	0.4	0.3	0.3
SD	0.42	0.19	0.14	0.19
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.4	0.2	0.9	0.5
8193	0.3	0.2	--	0.5
8181	0.3	0.1	0.0	0.2
8197	0.2	0.2	0.7	0.2
MEAN	0.3	0.2	0.5	0.4
SD	0.08	0.05	0.47	0.17
N	4	4	3	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.0	0.4	1.1	1.0
8213	0.2	0.2	0.2	0.4
8194	0.3	0.5	0.8	0.3
8182	0.5	0.5	0.6	1.4
MEAN	0.3	0.4	0.7	0.8
SD	0.21	0.14	0.38	0.52
N	4	4	4	4

(--)Data Unavailable

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: Eosinophil

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.2	0.2	0.2	0.1
8143	0.2	0.5	0.3	0.0
8148	0.1	0.5	0.3	0.5
8153	0.1	0.3	0.0	0.1
MEAN	0.2	0.4	0.2	0.2
SD	0.06	0.15	0.14	0.22
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	0.1	0.0	0.1	0.2
8170	0.3	0.1	0.4	0.2
8147	0.5	0.3	0.3	0.4
8151	0.2	0.2	0.4	0.1
MEAN	0.3	0.2	0.3	0.2
SD	0.17	0.13	0.14	0.13
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	0.5	0.7	0.5	0.4
8159	0.1	0.2	0.0	0.0
8175	0.2	0.3	0.1	0.0
8166	0.2	0.2	0.0	0.2
MEAN	0.3	0.4	0.2	0.2
SD	0.17	0.24	0.24	0.19
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	0.2	0.3	0.1	0.5
8156	0.2	0.1	0.1	0.1
8160	0.1	0.5	0.4	0.0
8144	0.3	0.0	0.1	0.4
MEAN	0.2	0.2	0.2	0.3
SD	0.08	0.22	0.15	0.24
N	4	4	4	4

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Eosinophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: Eosinophil

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.0	0.1	0.2	0.1
8214	0.2	0.2	0.3	0.2
8184	0.3	0.3	0.3	0.1
8180	0.3	0.3	0.0	0.4
MEAN	0.2	0.2	0.2	0.2
SD	0.14	0.10	0.14	0.14
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.1	0.1	0.0	0.0
8206	0.0	0.1	0.2	0.1
8185	0.2	0.2	0.3	0.3
8199	0.0	0.2	0.3	0.3
MEAN	0.1	0.2	0.2	0.2
SD	0.10	0.06	0.14	0.15
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.2	0.0	0.0	0.1
8193	0.2	0.2	--	0.3
8181	0.3	0.1	0.1	0.2
8197	0.1	0.6	0.2	0.2
MEAN	0.2	0.2	0.1	0.2
SD	0.08	0.26	0.10	0.08
N	4	4	3	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.5	0.1	0.0	0.2
8213	0.0	0.1	0.0	0.0
8194	0.1	0.2	0.2	0.0
8182	0.0	0.1	0.0	0.4
MEAN	0.2	0.1	0.1	0.2
SD	0.24	0.05	0.10	0.19
N	4	4	4	4

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: Basophils

SEX: MALE

UNITS:  $10^3/\text{cmm}$

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.0	0.0	0.0	0.0
8143	0.0	0.0	0.0	0.0
8148	0.0	0.0	0.0	0.0
8153	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	0.0	0.0	0.0	0.0
8170	0.0	0.0	0.0	0.0
8147	0.0	0.0	0.0	0.0
8151	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	0.0	0.0	0.0	0.0
8159	0.0	0.1	0.0	0.0
8175	0.0	0.0	0.0	0.0
8166	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.05	0.00	0.00
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	0.0	0.0	0.0	0.0
8156	0.0	0.0	0.0	0.0
8160	0.0	0.0	0.0	0.0
8144	0.0	0.0	0.7	0.0
MEAN	0.0	0.0	0.2	0.0
SD	0.00	0.00	0.35	0.00
N	4	4	4	4

WBC corrected for NRBC = or > 10

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Basophils

STUDY ID: 134  
STUDY NO: 134  
ABBR: Basophils

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.0	0.0	0.0	0.0
8214	0.0	0.0	0.0	0.0
8184	0.1	0.0	0.0	0.0
8180	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.05	0.00	0.00	0.00
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-F:0.1 mg base/kg/day				
8207	0.0	0.0	0.0	0.0
8206	0.0	0.0	0.0	0.0
8185	0.0	0.0	0.0	0.0
8199	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-F:0.3 mg base/kg/day				
8215	0.0	0.0	0.0	0.0
8193	0.4	0.0	--	0.0
8181	0.0	0.0	0.0	0.0
8197	0.0	0.0	0.0	0.0
MEAN	0.1	0.0	0.0	0.0
SD	0.20	0.00	0.00	0.00
N	4	4	3	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-F:1.0 mg base/kg/day				
8196	0.0	0.0	0.0	0.0
8213	0.0	0.0	0.0	0.0
8194	0.0	0.0	0.0	0.0
8182	0.0	0.0	0.0	0.0
MEAN	0.0	0.0	0.0	0.0
SD	0.00	0.00	0.00	0.00
N	4	4	4	4

(---)Data Unavailable

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Atypical Lymphocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: Atypical L

SEX: MALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	0.0	0.1	0.0	0.1
8143	0.0	0.0	0.4	0.0
8148	0.0	0.0	0.2	0.1
8153	0.1	0.0	0.1	0.1
MEAN	0.0	0.0	0.2	0.1
SD	0.05	0.05	0.17	0.05
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 2-M:0.1 mg base/kg/day				
8173	0.1	0.1	0.0	0.5
8170	0.1	0.0	0.0	0.1
8147	0.0	0.0	0.0	0.3
8151	0.0	0.2	0.1	0.1
MEAN	0.1	0.1	0.0	0.3
SD	0.06	0.10	0.05	0.19
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 3-M:0.3 mg base/kg/day				
8157	0.2	0.0	0.4	0.6
8159	0.1	0.0	0.1	0.3
8175	0.0	0.1	0.0	0.0
8166	0.3	0.2	0.4	0.2
MEAN	0.2	0.1	0.2	0.3
SD	0.13	0.10	0.21	0.25
N	4	4	4	4

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 4-M:1.0 mg base/kg/day				
8146	0.0	0.2	0.0	0.4
8156	0.0	0.1	0.1	0.0
8160	0.1	0.0	0.0	0.0
8144	0.0	0.1	0.0	0.3
MEAN	0.0	0.1	0.0	0.2
SD	0.05	0.08	0.05	0.21
N	4	4	4	4

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Atypical Lymphocytes

STUDY ID: 134  
STUDY NO: 134  
ABBR: Atypical L

SEX: FEMALE

UNITS:  $10^3/\text{cmm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	0.1	0.0	0.0	0.1
8214	0.1	0.1	0.1	0.0
8184	0.0	0.1	0.1	0.3
8180	0.0	0.4	0.3	0.4
MEAN	0.1	0.2	0.1	0.2
SD	0.06	0.17	0.13	0.18
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	0.0	0.1	0.0	0.2
8206	0.2	0.3	0.0	0.1
8185	0.0	0.0	0.4	0.3
8199	0.0	0.0	0.0	0.2
MEAN	0.1	0.1	0.1	0.2
SD	0.10	0.14	0.20	0.08
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	0.1	0.1	0.1	0.2
8193	0.0	0.2	--	0.0
8181	0.0	0.1	0.1	0.3
8197	0.1	0.2	0.2	0.3
MEAN	0.1	0.2	0.1	0.2
SD	0.06	0.06	0.06	0.14
N	4	4	3	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	0.0	0.2	0.4	0.1
8213	0.0	0.0	0.0	0.6
8194	0.0	0.1	0.3	0.3
8182	0.0	0.3	0.0	0.2
MEAN	0.0	0.2	0.2	0.3
SD	0.00	0.13	0.21	0.22
N	4	4	4	4

(--)Data Unavailable

WBC corrected for NRBC = or &gt; 10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8172	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	53	2.6	62	3.3	50	2.5	72	4.4
	I. Neutrophils	5	0.2	3	0.2	1	0.1	2	0.1
	Lymphocytes	35	1.7	25	1.3	42	2.1	21	1.3
	Monocytes	2	0.1	6	0.3	4	0.2	2	0.1
	Eosinophils	4	0.2	3	0.2	3	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.0	1	0.1	0	0.0	2	0.1
	WBC		4.9		5.3		5.0		6.1
8143	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	57	5.6	48	4.4	45	4.3	65	6.0
	I. Neutrophils	4	0.4	2	0.2	2	0.2	2	0.2
	Lymphocytes	36	3.5	43	4.0	42	4.0	33	3.0
	Monocytes	1	0.1	2	0.2	4	0.4	0	0.0
	Eosinophils	2	0.2	5	0.5	3	0.3	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	4	0.4	0	0.0
	WBC		9.8		9.2		9.6		9.2
8148	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	63	4.6	63	4.9	71	5.3	56	4.1
	I. Neutrophils	3	0.2	2	0.2	3	0.2	1	0.1
	Lymphocytes	31	2.3	27	2.1	19	1.4	34	2.5
	Monocytes	1	0.1	1	0.1	1	0.1	1	0.1
	Eosinophils	2	0.1	7	0.5	4	0.3	7	0.5
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	2	0.2	1	0.1
	WBC		7.3		7.7		7.5		7.4
8153	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	50	3.0	61	6.1	51	3.7	75	8.4
	I. Neutrophils	6	0.4	3	0.3	2	0.1	0	0.0
	Lymphocytes	39	2.3	29	2.9	41	3.0	16	1.8
	Monocytes	1	0.1	4	0.4	4	0.3	7	0.8
	Eosinophils	2	0.1	3	0.3	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	2	0.1	0	0.0	2	0.1	1	0.1
	WBC		5.9		10.0		7.2		11.2

NRBC Corrected After-10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 2-M : 0.1 mg base/kg/day

SEX: MALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8173	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	53	3.2	70	5.0	63	4.0	62	4.7
	I. Neutrophils	7	0.4	5	0.4	3	0.2	1	0.1
	Lymphocytes	31	1.9	22	1.6	31	2.0	27	2.0
	Monocytes	6	0.4	2	0.1	1	0.1	1	0.1
	Eosinophils	1	0.1	0	0.0	2	0.1	3	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	2	0.1	1	0.1	0	0.0	6	0.5
	WBC		6.1		7.2		6.4		7.5
8170	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	59	3.1	54	3.2	67	6.0	50	3.0
	I. Neutrophils	3	0.2	6	0.4	0	0.0	5	0.3
	Lymphocytes	29	1.5	38	2.2	23	2.0	40	2.4
	Monocytes	2	0.1	0	0.0	6	0.5	1	0.1
	Eosinophils	6	0.3	2	0.1	4	0.4	3	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	0	0.0	0	0.0	1	0.1
	WBC		5.2		5.9		8.9		6.0
8147	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	61	4.6	71	7.2	57	5.1	60	3.7
	I. Neutrophils	4	0.3	3	0.3	2	0.2	3	0.2
	Lymphocytes	26	2.0	16	1.6	38	3.4	24	1.5
	Monocytes	2	0.2	7	0.7	0	0.0	1	0.1
	Eosinophils	7	0.5	3	0.3	3	0.3	7	0.4
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0	5	0.3
	WBC		7.6		10.2		8.9		6.1
8151	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	56	4.6	67	6.3	56	4.9	59	5.8
	I. Neutrophils	2	0.2	2	0.2	1	0.1	2	0.2
	Lymphocytes	31	2.5	25	2.4	36	3.2	32	3.2
	Monocytes	8	0.7	2	0.2	2	0.2	5	0.5
	Eosinophils	3	0.2	2	0.2	4	0.4	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	2	0.2	1	0.1	1	0.1
	WBC		8.2		9.4		8.8		9.9

NRBC Corrected After-10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 3-M : 0.3 mg base/kg/day

SEX: MALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8157	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	53	5.6	67	12.1	46	4.3	48	4.4
	I. Neutrophils	7	0.7	1	0.2	1	0.1	1	0.1
	Lymphocytes	31	3.3	17	3.1	39	3.7	33	3.0
	Monocytes	2	0.2	11	2.0	5	0.5	8	0.7
	Eosinophils	5	0.5	4	0.7	5	0.5	4	0.4
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	2	0.2	0	0.0	4	0.4	6	0.6
	WBC		10.5		18.1		9.4		9.2
8159	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	71	6.3	64	5.0	72	5.5	71	6.2
	I. Neutrophils	11	1.0	6	0.5	4	0.3	6	0.5
	Lymphocytes	14	1.2	25	2.0	22	1.7	11	1.0
	Monocytes	2	0.2	1	0.1	1	0.1	9	0.8
	Eosinophils	1	0.1	3	0.2	0	0.0	0	0.0
	Basophils	0	0.0	1	0.1	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	0	0.0	1	0.1	3	0.3
	WBC		8.9		7.8		7.6		8.7
8175	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	70	6.0	61	6.0	72	7.2	77	8.0
	I. Neutrophils	7	0.6	5	0.5	1	0.1	3	0.3
	Lymphocytes	12	1.0	24	2.4	22	2.2	11	1.1
	Monocytes	9	0.8	6	0.6	4	0.4	9	0.9
	Eosinophils	2	0.2	3	0.3	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	0	0.0	0	0.0
	WBC		8.5		9.8		10.0		10.4
8166	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	62	5.5	74	7.3	77	6.6	71	5.3
	I. Neutrophils	6	0.5	2	0.2	2	0.2	3	0.2
	Lymphocytes	22	2.0	16	1.6	14	1.2	17	1.3
	Monocytes	5	0.4	4	0.4	2	0.2	5	0.4
	Eosinophils	2	0.2	2	0.2	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	3	0.3	2	0.2	5	0.4	2	0.2
	WBC		8.9		9.8		8.6		7.5

NRBC Corrected After-10

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 4-M : 1.0 mg base/kg/day

SEX: MALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8146	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	66	5.0	72	6.2	57	3.8	65	5.1
	I. Neutrophils	5	0.4	1	0.1	3	0.2	2	0.2
	Lymphocytes	22	1.7	10	0.9	29	1.9	10	0.8
	Monocytes	4	0.3	11	0.9	10	0.7	12	0.9
	Eosinophils	3	0.2	4	0.3	1	0.1	6	0.5
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	2	0.2	0	0.0	5	0.4
	WBC		7.5		8.6		6.7		7.8
8156	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60	4.6	68	6.2	47	2.8	67	5.9
	I. Neutrophils	5	0.4	6	0.5	3	0.2	5	0.4
	Lymphocytes	23	1.7	23	2.1	32	1.9	22	1.9
	Monocytes	10	0.8	1	0.1	15	0.9	5	0.4
	Eosinophils	2	0.2	1	0.1	2	0.1	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	1	0.1	0	0.0
	WBC		7.6		9.1		5.9		8.8
8160	Nucleated Red Cells	0		0		0		1	
	M. Neutrophils	77	6.5	61	5.5	70	6.7	73	8.0
	I. Neutrophils	2	0.2	2	0.2	2	0.2	3	0.3
	Lymphocytes	17	1.4	21	1.9	20	1.9	16	1.8
	Monocytes	2	0.2	11	1.0	4	0.4	8	0.9
	Eosinophils	1	0.1	5	0.5	4	0.4	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	0	0.0	0	0.0	0	0.0
	WBC		8.5		9.0		9.5		11.0
8144	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	70	6.1	66	4.4	61	6.8	71	6.2
	I. Neutrophils	8	0.7	3	0.2	4	0.4	3	0.3
	Lymphocytes	18	1.6	30	2.0	18	2.0	14	1.2
	Monocytes	1	0.1	0	0.0	10	1.1	5	0.4
	Eosinophils	3	0.3	0	0.0	1	0.1	4	0.4
	Basophils	0	0.0	0	0.0	6	0.7	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	0	0.0	3	0.3
	WBC		8.7		6.6		11.1		8.8

NRBC Corrected After-10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8211	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	72	5.9	62	4.5	63	4.7	66	5.0
	I. Neutrophils	2	0.2	3	0.2	3	0.2	4	0.3
	Lymphocytes	21	1.7	30	2.2	29	2.2	23	1.7
	Monocytes	4	0.3	3	0.2	3	0.2	5	0.4
	Eosinophils	0	0.0	2	0.1	2	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	0	0.0	0	0.0	1	0.1
	WBC		8.2		7.3		7.5		7.6
8214	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	61	4.7	65	5.1	71	5.5	68	6.5
	I. Neutrophils	1	0.1	5	0.4	1	0.1	4	0.4
	Lymphocytes	22	1.7	23	1.8	17	1.3	22	2.1
	Monocytes	13	1.0	4	0.3	6	0.5	4	0.4
	Eosinophils	2	0.2	2	0.2	4	0.3	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	1	0.1	1	0.1	0	0.0
	WBC		7.7		7.9		7.8		9.6
8184	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	58	6.3	64	6.5	74	6.8	74	7.1
	I. Neutrophils	0	0.0	1	0.1	1	0.1	3	0.3
	Lymphocytes	36	3.9	25	2.6	19	1.7	18	1.7
	Monocytes	2	0.2	6	0.6	2	0.2	1	0.1
	Eosinophils	3	0.3	3	0.3	3	0.3	1	0.1
	Basophils	1	0.1	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	1	0.1	3	0.3
	WBC		10.8		10.2		9.2		9.6
8180	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	68	9.1	60	6.2	64	6.8	52	3.7
	I. Neutrophils	4	0.5	1	0.1	1	0.1	2	0.1
	Lymphocytes	23	3.1	26	2.7	30	3.2	30	2.1
	Monocytes	3	0.4	6	0.6	2	0.2	5	0.4
	Eosinophils	2	0.3	3	0.3	0	0.0	6	0.4
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	4	0.4	3	0.3	5	0.4
	WBC		13.4		10.4		10.6		7.1

NRBC Corrected After-10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 2-F : 0.1 mg base/kg/day

SEX: FEMALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8207	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	64	6.0	59	6.1	65	8.4	71	6.4
	I. Neutrophils	6	0.6	1	0.1	4	0.5	2	0.2
	Lymphocytes	26	2.4	34	3.5	29	3.7	24	2.2
	Monocytes	3	0.3	4	0.4	2	0.3	1	0.1
	Eosinophils	1	0.1	1	0.1	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	0	0.0	2	0.2
	WBC		9.3		10.4		12.9		9.0
8206	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	67	6.4	71	6.5	75	8.9	69	4.8
	I. Neutrophils	1	0.1	0	0.0	4	0.5	0	0.0
	Lymphocytes	28	2.7	22	2.0	16	1.9	27	1.9
	Monocytes	2	0.2	3	0.3	3	0.4	1	0.1
	Eosinophils	0	0.0	1	0.1	2	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	2	0.2	3	0.3	0	0.0	2	0.1
	WBC		9.6		9.1		11.8		6.9
8185	Nucleated Red Cells	0		0		0		1	
	M. Neutrophils	68	5.5	78	12.2	74	7.5	56	3.9
	I. Neutrophils	2	0.2	1	0.2	3	0.3	2	0.1
	Lymphocytes	23	1.9	18	2.8	12	1.2	27	1.9
	Monocytes	4	0.3	2	0.3	4	0.4	7	0.5
	Eosinophils	3	0.2	1	0.2	3	0.3	4	0.3
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	4	0.4	4	0.3
	WBC		8.1		15.6		10.2		6.9
8199	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	75	6.8	66	5.1	72	5.7	68	4.4
	I. Neutrophils	1	0.1	0	0.0	1	0.1	1	0.1
	Lymphocytes	12	1.1	22	1.7	22	1.7	20	1.3
	Monocytes	12	1.1	9	0.7	1	0.1	4	0.3
	Eosinophils	0	0.0	3	0.2	4	0.3	4	0.3
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0	3	0.2
	WBC		9.1		7.7		7.9		6.4

NRBC Corrected After-10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

## WHITE DIFFERENTIAL DATA

STUDY ID: 134

STUDY NO: 134

GROUP: 3-F : 0.3 mg base/kg/day

SEX: FEMALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8215	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	51	3.6	64	5.2	66	6.5	48	3.6
	I. Neutrophils	5	0.4	2	0.2	0	0.0	0	0.0
	Lymphocytes	34	2.4	31	2.5	24	2.4	43	3.3
	Monocytes	6	0.4	2	0.2	9	0.9	6	0.5
	Eosinophils	3	0.2	0	0.0	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	1	0.1	1	0.1	1	0.1	2	0.2
	WBC		7.1		8.2		9.9		7.6
8193	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	60	5.6	62	5.4	52	4.2	59	6.0
	I. Neutrophils	1	0.1	2	0.2	2	0.2	1	0.1
	Lymphocytes	30	2.8	30	2.6	40	3.2	32	3.2
	Monocytes	3	0.3	2	0.2	2	0.2	5	0.5
	Eosinophils	2	0.2	2	0.2	4	0.3	3	0.3
	Basophils	4	0.4	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	2	0.2	0	0.0	0	0.0
	WBC		9.3		8.7		8.1		10.1
8181	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	56	4.0	73	8.8	72	6.3	55	4.2
	I. Neutrophils	1	0.1	0	0.0	1	0.1	0	0.0
	Lymphocytes	35	2.5	24	2.9	25	2.2	36	2.7
	Monocytes	4	0.3	1	0.1	0	0.0	3	0.2
	Eosinophils	4	0.3	1	0.1	1	0.1	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	1	0.1	4	0.3
	WBC		7.1		12.0		8.7		7.6
8197	Nucleated Red Cells	0		0		0		0	
	M. Neutrophils	64	4.6	62	6.7	74	6.9	74	5.2
	I. Neutrophils	2	0.1	5	0.5	3	0.3	0	0.0
	Lymphocytes	28	2.0	23	2.5	12	1.1	16	1.1
	Monocytes	3	0.2	2	0.2	7	0.7	3	0.2
	Eosinophils	1	0.1	6	0.6	2	0.2	3	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	2	0.1	2	0.2	2	0.2	4	0.3
	WBC		7.2		10.8		9.3		7.0

NRBC Corrected After-10

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 134  
STUDY NO: 134

GROUP: 4-F : 1.0 mg base/kg/day

SEX: FEMALE

ANIMAL ID		Week -3		Wk -2/-1		Week 2		Week 5	
		REL	ABS	REL	ABS	REL	ABS	REL	ABS
8196	Nucleated Red Cells	0		0		0		1	
	M. Neutrophils	52	4.8	49	4.1	60	5.5	47	3.5
	I. Neutrophils	2	0.2	4	0.3	2	0.2	0	0.0
	Lymphocytes	41	3.8	39	3.3	22	2.0	37	2.8
	Monocytes	0	0.0	5	0.4	12	1.1	13	1.0
	Eosinophils	5	0.5	1	0.1	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	2	0.2	4	0.4	1	0.1
	WBC		9.2		8.4		9.1		7.5
8213	Nucleated Red Cells	0		0		0		5	
	M. Neutrophils	62	4.4	57	4.0	64	5.2	55	3.7
	I. Neutrophils	6	0.4	6	0.4	4	0.3	8	0.5
	Lymphocytes	29	2.1	33	2.3	29	2.3	22	1.5
	Monocytes	3	0.2	3	0.2	3	0.2	6	0.4
	Eosinophils	0	0.0	1	0.1	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0	9	0.6
	WBC		7.1		7.0		8.1		6.7
8194	Nucleated Red Cells	0		0		1		0	
	M. Neutrophils	65	9.2	63	6.8	69	6.5	68	6.3
	I. Neutrophils	3	0.4	0	0.0	1	0.1	4	0.4
	Lymphocytes	29	4.1	29	3.1	17	1.6	22	2.0
	Monocytes	2	0.3	5	0.5	8	0.8	3	0.3
	Eosinophils	1	0.1	2	0.2	2	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	1	0.1	3	0.3	3	0.3
	WBC		14.2		10.8		9.4		9.2
8182	Nucleated Red Cells	0		0		4		0	
	M. Neutrophils	64	4.9	64	6.0	76	11.2	67	6.2
	I. Neutrophils	1	0.1	2	0.2	4	0.6	1	0.1
	Lymphocytes	29	2.2	25	2.4	16	2.4	11	1.0
	Monocytes	6	0.5	5	0.5	4	0.6	15	1.4
	Eosinophils	0	0.0	1	0.1	0	0.0	4	0.4
	Basophils	0	0.0	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	3	0.3	0	0.0	2	0.2
	WBC		7.6		9.4		14.8		9.3

NRBC Corrected After-10

LABCAT HE4.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: PlateletsSTUDY ID: 134  
STUDY NO: 134  
ABBR: PLT

SEX: MALE

UNITS:  $10^3/\text{ccm}$ 

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	309	317	314	282
8143	289	271	224	290
8148	323	313	275	287
8153	367	300	301	358
MEAN	322	300	279	304
SD	33.1	20.8	39.8	36.0
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	281	319	257	277
8170	348	379	376	301
8147	447	402	417	354
8151	379	389	340	351
MEAN	364	372	348	321
SD	68.9	36.7	68.0	38.0
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	289	235	176	112
8159	244	256	172	103
8175	371	308	218	169
8166	272	240	194	125
MEAN	294	260	190	127
SD	54.6	33.4	21.0	29.3
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	333	273	147	143
8156	403	365	130	141
8160	419	374	234	87
8144	333	195	56	174
MEAN	372	302	142	136
SD	45.5	84.5	73.1	36.1
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Platelets

STUDY ID: 134  
STUDY NO: 134  
ABBR: PLT

SEX: FEMALE

UNITS:  $10^3/\text{ccm}$

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	237	255	202	235
8214	309	332	334	344
8184	533	453	451	453
8180	284	304	200	263
MEAN	341	336	297	324
SD	131.6	84.2	120.4	97.8
N	4	4	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	285	287	308	244
8206	334	334	278	331
8185	383	389	419	309
8199	309	379	302	345
MEAN	328	347	327	307
SD	41.9	46.8	62.9	44.7
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	340	322	305	216
8193	198	158	172	142
8181	278	259	216	143
8197	340	332	232	119
MEAN	289	268	231	155
SD	67.3	80.0	55.3	42.2
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	301	277	115	100
8213	302	307	159	87
8194	383	348	220	136
8182	337	365	318	148
MEAN	331	324	203	118
SD	38.6	39.8	87.9	28.9
N	4	4	4	4

LABCAT HE4.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Prothrombin Time

STUDY ID: 134  
STUDY NO: 134  
ABBR: PT

SEX: MALE

UNITS: sec

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	7.1	6.9	6.9	7.1
8143	7.3	7.4	7.3	7.7
8148	7.0	6.9	7.0	7.4
8153	7.0	7.0	7.1	7.2
MEAN	7.1	7.1	7.1	7.4
SD	0.14	0.24	0.17	0.26
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	7.4	7.4	7.4	7.7
8170	7.9	7.8	7.6	7.9
8147	7.1	7.0	6.8	7.1
8151	7.7	7.6	7.6	7.8
MEAN	7.5	7.5	7.4	7.6
SD	0.35	0.34	0.38	0.36
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	6.9	6.7	6.9	6.9
8159	6.9	7.1	7.1	7.1
8175	7.0	6.8	6.8	7.1
8166	7.1	7.0	7.0	7.2
MEAN	7.0	6.9	7.0	7.1
SD	0.10	0.18	0.13	0.13
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	7.2	7.1	6.9	7.1
8156	7.0	6.9	6.8	6.8
8160	6.9	6.8	6.9	7.0
8144	7.0	6.8	6.7	7.0
MEAN	7.0	6.9	6.8	7.0
SD	0.13	0.14	0.10	0.13
N	4	4	4	4

LABCAT HE4.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Prothrombin Time

STUDY ID: 134  
STUDY NO: 134  
ABBR: PT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	7.3	7.1	7.1	7.5
8214	7.1	--	6.9	7.5
8184	7.2	7.2	7.1	7.2
8180	6.8	7.0	11.2	7.3
MEAN	7.1	7.1	8.1	7.4
SD	0.22	0.10	2.09	0.15
N	4	3	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	7.5	7.5	7.2	7.4
8206	7.5	7.2	7.0	7.3
8185	7.5	7.1	7.2	7.5
8199	6.7	7.4	7.0	7.6
MEAN	7.3	7.3	7.1	7.5
SD	0.40	0.18	0.12	0.13
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	7.5	6.9	6.9	7.1
8193	7.2	7.3	7.2	7.2
8181	7.2	6.8	7.1	7.2
8197	7.2	6.9	6.8	7.1
MEAN	7.3	7.0	7.0	7.2
SD	0.15	0.22	0.18	0.06
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	7.5	7.5	7.0	7.0
8213	7.5	7.3	6.9	7.1
8194	7.3	7.6	7.2	7.3
8182	7.2	6.9	6.7	6.9
MEAN	7.4	7.3	7.0	7.1
SD	0.15	0.31	0.21	0.17
N	4	4	4	4

(--)-Data Unavailable

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Act. Partial Thrombo. Time

STUDY ID: 134  
STUDY NO: 134  
ABBR: APTT

SEX: MALE

UNITS: sec

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-M:0 mg base/kg/day				
8172	11.7	11.4	11.1	12.1
8143	11.6	11.6	11.6	11.2
8148	11.0	11.0	10.6	10.6
8153	11.6	11.7	11.1	11.6
MEAN	11.5	11.4	11.1	11.4
SD	0.32	0.31	0.41	0.63
N	4	4	4	4

GROUP: 2-M:0.1 mg base/kg/day				
8173	12.2	12.1	11.8	9.9
8170	12.2	12.1	12.6	12.9
8147	11.5	11.4	11.0	11.8
8151	12.2	11.5	12.2	12.5
MEAN	12.0	11.8	11.9	11.8
SD	0.35	0.38	0.68	1.33
N	4	4	4	4

GROUP: 3-M:0.3 mg base/kg/day				
8157	12.0	12.4	12.3	11.9
8159	13.8	11.8	12.5	12.8
8175	12.3	12.7	12.1	12.6
8166	12.2	12.0	11.3	11.6
MEAN	12.6	12.2	12.1	12.2
SD	0.83	0.40	0.53	0.57
N	4	4	4	4

GROUP: 4-M:1.0 mg base/kg/day				
8146	11.6	12.2	11.3	11.5
8156	11.5	11.3	11.1	12.2
8160	12.6	12.4	12.4	13.5
8144	12.1	12.0	11.6	12.0
MEAN	12.0	12.0	11.6	12.3
SD	0.51	0.48	0.57	0.85
N	4	4	4	4

LABCAT HE4.26

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP  
TEST: Act. Partial Thrombo. Time

STUDY ID: 134  
STUDY NO: 134  
ABBR: APTT

SEX: FEMALE

UNITS: sec

ANIMAL ID	Week -3	Wk -2/-1	Week 2	Week 5
GROUP: 1-F:0 mg base/kg/day				
8211	11.7	11.3	11.1	11.4
8214	13.4	--	13.0	13.9
8184	11.3	11.9	12.3	12.4
8180	11.7	11.6	6.8	11.2
MEAN	12.0	11.6	10.8	12.2
SD	0.94	0.30	2.78	1.23
N	4	3	4	4

GROUP: 2-F:0.1 mg base/kg/day				
8207	12.5	11.3	11.2	11.6
8206	13.2	12.5	13.3	13.5
8185	11.1	12.1	11.1	11.0
8199	12.7	12.2	12.0	12.0
MEAN	12.4	12.0	11.9	12.0
SD	0.90	0.51	1.02	1.07
N	4	4	4	4

GROUP: 3-F:0.3 mg base/kg/day				
8215	12.6	13.0	12.6	13.1
8193	11.9	11.3	11.2	11.3
8181	12.0	12.6	11.6	11.7
8197	11.8	11.4	11.2	12.2
MEAN	12.1	12.1	11.7	12.1
SD	0.36	0.85	0.66	0.78
N	4	4	4	4

GROUP: 4-F:1.0 mg base/kg/day				
8196	12.6	11.9	12.7	12.3
8213	11.9	11.4	11.2	11.7
8194	12.3	11.7	11.6	13.6
8182	11.8	12.0	11.5	12.0
MEAN	12.2	11.8	11.8	12.4
SD	0.37	0.26	0.66	0.84
N	4	4	4	4

(--)-Data Unavailable

LABCAT HE4.26

DRAFT

APPENDIX 8  
Individual Urinalysis Data

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

Male Urinalysis Data (Week 5)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	APP	SG	COL	NIT	LEU	pH	PRO	GLU	KET	URO	BILI	BLOOD Ery/ul
0	8172	CLOUDY	1.060	Y	NEG	1+	7	TRACE	NOR	NEG	NOR	NEG	2+
	8143	CLEAR	1.015	LY	POS	NEG	8	TRACE	NOR	NEG	NOR	NEG	NEG
	8148	CLOUDY	1.072	Y	POS	1+	7	TRACE	NOR	NEG	NOR	NEG	1+
	8153	HAZY	1.066	DY	NEG	2+	7	1+	NOR	NEG	NOR	NEG	1+
0.1	8173	HAZY	1.033	Y	NEG	1+	7	1+	NOR	NEG	NOR	NEG	NEG
	8170	TURBID	1.006	Y	POS	1+	8	1+	NOR	NEG	NOR	NEG	3+
	8147	HAZY	1.075	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8151	HAZY	1.052	DY	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	1+
0.3	8157	HAZY	1.078	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	2+
	8159	HAZY	1.056	Y	NEG	NEG	6	1+	NOR	NEG	NOR	NEG	NEG
	8175	HAZY	1.084	DY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8166	HAZY	1.075	DY	NEG	NEG	6	2+	NOR	NEG	NOR	NEG	1+
1.0	8146	HAZY	1.075	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	NEG
	8156	CLEAR	1.066	DY	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8160	HAZY	1.072	AM	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8144	HAZY	1.027	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG

# DRAFT

UIC/TRL Study No. 134

## FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

### Male Urinalysis Data (Week 5)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL CELLS SQ TRANS RENAL			CRYSTALS	BACTERIA	SPERM	MUCUS
0	8172	HY 2	20	13	3	0	0	TP 1+	2+	1+	0
	8143	0	0	0	0	0	0	TP 0	1+	0	0
	8148	FG 2 CG 1	10	5	3	0	0	TP 2+	2+	0	0
	8153	FG 2 HY 1	5	23	1	0	0	TP 1+	0	1+	0
0.1	8173	HY 1	0	5	4	0	0	TP 1+	2+	1+	0
	8170	FG 1	20	10	2	0	0	TP 1+	1+	0	0
	8147	HY 3 FG 1	0	13	2	0	0	TP 1+	1+	2+	0
	8151	HY 1	5	15	2	0	0	TP 0	1+	1+	0
0.3	8157	HY 1	3	0	1	0	0	TP 0	1+	1+	0
	8159	CG 1	0	0	2	0	0	TP 2+	1+	2+	0
	8175	FG 3	0	13	0	0	0	TP 1+	1+	1+	0
	8166	HY 2 FG 1	7	30	4	0	0	TP 1+	2+	1+	0
1.0	8146	FG 1	1	5	1	0	0	TP 3+	1+	2+	0
	8156	HY 2 CG FG 1	0	25	3	0	0	TP 1+	1+	1+	0
	8160	HY 4 CG	0	5	2	0	0	TP 0	1+	1+	0
	8144	0	0	0	3	0	0	TP 0	1+	1+	0

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

Female Urinalysis Data (Week 5)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	APP	SG	COL	NIT	LEU	pH	PRO	GLU	KET	URO	BILI	BLOOD Ery/ul
0	8211	CLEAR	1.044	Y	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8214	CLEAR	1.072	DY	NEG	NEG	6	NEG	NOR	NEG	NOR	NEG	2+
	8184	HAZY	1.072	DY	POS	2+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8180	HAZY	1.066	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	1+
0.1	8207	HAZY	1.090	DY	NEG	1+	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8206	HAZY	1.062	DY	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	NEG
	8185	CLEAR	1.018	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	2+
	8199	HAZY	1.054	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
0.3	8215	HAZY	1.054	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8193	CLEAR	1.030	Y	NEG	NEG	7	TRACE	NOR	NEG	NOR	NEG	2+
	8181	HAZY	1.066	DY	NEG	2+	6	TRACE	NOR	NEG	NOR	NEG	2+
	8197	HAZY	1.093	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
1.0	8196	HAZY	1.078	DY	NEG	NEG	6	TRACE	NOR	NEG	NOR	NEG	1+
	8213	HAZY	1.034	Y	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG
	8194	TURBID	1.012	Y	NEG	TRACE	6	TRACE	NOR	NEG	NOR	NEG	3+
	8182	HAZY	1.124	AM	POS	NEG	6	TRACE	NOR	NEG	NOR	NEG	NEG

# DRAFT

UIC/TRL Study No. 134

## FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

### Female Urinalysis Data (Week 5)

DOSE LEVEL (mg base/kg/day)	ANIMAL NO.	CASTS	RBC	WBC	EPITHELIAL SQ	CELLS TRANS	RENAL	CRYSTALS	BACTERIA	SPERM	MUCUS
0	8211	FG 1 HY 1	0	0	5	10	0	TP 0	1+	0	0
	8214	HY 1	15	10	5	3	0	TP 1+	1+	0	0
	8184	HY 8 FG 1	0	32	7	2	0	TP 1+	1+	0	0
	8180	FG 2 HY 1	4	10	4	0	0	TP 1+	1+	0	0
0.1	8207	HY 4 FG 2	0	4	2	0	0	TP 1+	1+	0	0
	8206	HY 1 FG 1	0	0	9	0	0	TP 2+	1+	0	0
	8185	FG 1	10	0	2	0	0	TP 0	1+	0	0
	8199	HY 3 FG 1	0	15	5	10	0	TP 0	1+	0	0
0.3	8215	HY 1	0	2	4	0	0	TP 0	1+	0	0
	8193	0	15	0	5	0	0	TP 1+	1+	0	0
	8181	HY 2 FG 1	15	75	4	2	0	TP 2+	1+	0	0
	8197	HY 5	0	15	5	3	0	TP 0	1+	0	0
1.0	8196	HY 7	5	0	5	1	0	TP 3+	1+	0	0
	8213	FG 2 HY 1	0	0	3	0	0	TP 0	2+	0	0
	8194	FG 2	10	5	0	0	0	TP 0	2+	0	0
	8182	HY 1	0	0	50	0	0	TP 1+	1+	0	0

DRAFT

APPENDIX 9  
Cardiology Report



Department of Veterinary  
Physiology and Pharmacology

1900 Coffey Road  
Columbus, OH 43210-1092  
Phone 614-292-1391

Fax 614-292-2011

**DRAFT**

August 13, 1994

TO: Dr. Barry S. Levine  
Director  
Toxicology Research Laboratory  
1940 West Taylor Street  
Chicago, Illinois 60612-7353

FROM: Robert L. Hamlin, DVM, PhD  
Diplomate ACVIM (Cardiology/Internal Medicine)  
1520 Grenoble Road  
Columbus, Ohio 43221

RE: Report on ECGs for UIC/TRL Study #134, Four Week Oral Toxicity Study  
of WR242511 in Dogs.

All dogs at all doses and at both recording times had ECGs that were within limits of normal. No dog manifested rhythm disturbance. In Week 4, the PR interval was longer for female dogs in group 3 (0.3 mg base/kg/day) than for controls; however it was not longer than for the same group during the pretest period, nor was the PR interval prolonged in the group receiving the highest dose. Therefore, there are no systematic changes in the ECGs that could be attributable to the compound.



FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

Electrocardiogram Diagnosis of Males

DRAFT

Dose	Animal Number	Pretest	Week 4
0	8172	WNL	WNL
	8143	WNL	WNL
	8148	WNL	WNL
	8153	WNL	WNL
0.1	8173	WNL (LAD)	WNL
	8170	WNL (LAD)	WNL
	8147	WNL	WNL
	8151	WNL	WNL
0.3	8157	WNL	WNL
	8159	WNL	WNL
	8175	WNL	WNL
	8166	WNL	WNL
1.0	8146	WNL	WNL (RAD)
	8156	WNL	WNL
	8160	WNL	WNL
	8144	WNL (RAD)	WNL (IVCD)

DOSE = mg base/kg/day

WNL = Within normal limits

PWNL = Probably within normal limits

RAD = Right axis deviation

LAD = Left axis deviation

IVCD = Intraventricular conduction defect

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

Electrocardiogram Diagnosis of Females

Dose	Animal Number	Pretest	Week 4
0	8211	WNL	WNL
	8214	WNL	WNL
	8184	WNL	WNL (RAD)
	8180	WNL (RAD)	WNL (IVCD)
0.1	8207	WNL (LAD)	WNL
	8206	WNL	WNL
	8185	WNL	WNL
	8199	WNL	WNL (RAD)
0.3	8215	WNL	WNL
	8193	WNL	WNL
	8181	WNL	WNL
	8197	WNL	WNL
1.0	8196	WNL	WNL
	8213	WNL	WNL
	8194	WNL	WNL
	8182	WNL	WNL

DOSE = mg base/kg/day

WNL = Within normal limits

PWNL = Probably within normal limits

RAD = Right axis deviation

LAD = Left axis deviation

IVCD = Intraventricular conduction defect

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: Heart Rate

STUDY ID: 134  
STUDY NO: 134  
ABBR: HR

SEX: MALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-M : 0 mg base/kg/day  
MEAN                      118                      120  
SD                        25.1                      19.9  
N                          4                          4

Group: 2-M : 0.1 mg base/kg/day  
MEAN                      133                      123  
SD                        23.0                      13.5  
N                          4                          4

Group: 3-M : 0.3 mg base/kg/day  
MEAN                      117                      120  
SD                        26.6                      32.5  
N                          4                          4

Group: 4-M : 1.0 mg base/kg/day  
MEAN                      132                      118  
SD                        22.7                      23.2  
N                          4                          4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: Heart Rate

STUDY ID: 134  
STUDY NO: 134  
ABBR: HR

SEX: FEMALE

UNITS: bpm

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-F : 0 mg base/kg/day

MEAN	125	98
SD	23.9	10.9
N	4	4

Group: 2-F : 0.1 mg base/kg/day

MEAN	117	101
SD	28.0	25.1
N	4	4

Group: 3-F : 0.3 mg base/kg/day

MEAN	136	111
SD	26.1	18.7
N	4	4

Group: 4-F : 1.0 mg base/kg/day

MEAN	90	90
SD	28.5	29.9
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: P Wave Duration

STUDY ID: 134  
STUDY NO: 134  
ABBR: P

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-M : 0 mg base/kg/day

MEAN	40	42
SD	1.5	2.6
N	4	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	41	40
SD	4.8	5.0
N	4	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	40	38
SD	4.2	1.3
N	4	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	40	41
SD	1.3	0.5
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: P Wave Duration

STUDY ID: 134  
STUDY NO: 134  
ABBR: P

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-F : 0 mg base/kg/day  
MEAN                      40                      41  
SD                        2.9                      3.1  
N                          4                          4

Group: 2-F : 0.1 mg base/kg/day  
MEAN                      41                      42  
SD                        4.7                      4.5  
N                          4                          4

Group: 3-F : 0.3 mg base/kg/day  
MEAN                      41                      43  
SD                        2.1                      3.9  
N                          4                          4

Group: 4-F : 1.0 mg base/kg/day  
MEAN                      41                      41  
SD                        8.8                      5.8  
N                          4                          4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: PR Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: PR

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-M : 0 mg base/kg/day

MEAN	100	95
SD	3.7	2.6
N	4	4

Group: 2-M : 0.1 mg base/kg/day

MEAN	109	108
SD	11.1	9.8
N	4	4

Group: 3-M : 0.3 mg base/kg/day

MEAN	96	85
SD	4.8	5.4
N	4	4

Group: 4-M : 1.0 mg base/kg/day

MEAN	94	92
SD	10.4	10.6
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: PR Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: PR

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-F : 0 mg base/kg/day  
MEAN                      97                      92  
SD                        6.3                      4.5  
N                          4                          4

Group: 2-F : 0.1 mg base/kg/day  
MEAN                      102                      94  
SD                        11.2                      7.2  
N                          4                          4

Group: 3-F : 0.3 mg base/kg/day  
MEAN                      110                      110\*  
SD                        11.4                      11.0  
N                          4                          4

Group: 4-F : 1.0 mg base/kg/day  
MEAN                      100                      95  
SD                        7.3                      4.2  
N                          4                          4

\*-Significant Difference from Control P < .05

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: QRS Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QRS

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 4

Group: 1-M : 0 mg base/kg/day  
MEAN 39 40  
SD 2.2 1.7  
N 4 4

Group: 2-M : 0.1 mg base/kg/day  
MEAN 42 41  
SD 3.4 2.2  
N 4 4

Group: 3-M : 0.3 mg base/kg/day  
MEAN 39 40  
SD 2.4 1.6  
N 4 4

Group: 4-M : 1.0 mg base/kg/day  
MEAN 38 38  
SD 0.8 1.6  
N 4 4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: QRS Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QRS

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-F : 0 mg base/kg/day  
MEAN                      37                      43  
SD                        2.6                      3.0  
N                          4                          4

Group: 2-F : 0.1 mg base/kg/day  
MEAN                      40                      40  
SD                        3.2                      1.7  
N                          4                          4

Group: 3-F : 0.3 mg base/kg/day  
MEAN                      39                      44  
SD                        1.3                      3.6  
N                          4                          4

Group: 4-F : 1.0 mg base/kg/day  
MEAN                      37                      38  
SD                        2.6                      1.9  
N                          4                          4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: QT Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QT

SEX: MALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s):      Pretest      Week 4

Group: 1-M : 0 mg base/kg/day  
MEAN                      194                      197  
SD                        24.6                      16.1  
N                          4                          4

Group: 2-M : 0.1 mg base/kg/day  
MEAN                      189                      185  
SD                        11.0                      12.1  
N                          4                          4

Group: 3-M : 0.3 mg base/kg/day  
MEAN                      213                      199  
SD                        13.3                      12.6  
N                          4                          4

Group: 4-M : 1.0 mg base/kg/day  
MEAN                      179                      185  
SD                        7.9                        16.9  
N                          4                          4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

SUMMARY OF CARDIOLOGY TESTS  
TEST: QT Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QT

SEX: FEMALE

UNITS: ms

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Pretest Week 4

Group: 1-F : 0 mg base/kg/day  
MEAN 188 194  
SD 30.8 13.1  
N 4 4

Group: 2-F : 0.1 mg base/kg/day  
MEAN 196 194  
SD 24.7 17.5  
N 4 4

Group: 3-F : 0.3 mg base/kg/day  
MEAN 204 182  
SD 13.0 14.3  
N 4 4

Group: 4-F : 1.0 mg base/kg/day  
MEAN 213 200  
SD 11.6 6.2  
N 4 4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: Heart Rate

STUDY ID: 134  
STUDY NO: 134  
ABBR: HR

SEX: MALE

UNITS: bpm

ANIMAL ID    Pretest    Week 4

GROUP: 1-M:0 mg base/kg/day

8172	94	95
8143	109	114
8148	153	141
8153	115	129

MEAN	118	120
SD	25.1	19.9
N	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	99	109
8170	137	138
8147	150	114
8151	144	130

MEAN	133	123
SD	23.0	13.5
N	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	153	162
8159	91	94
8175	105	95
8166	120	130

MEAN	117	120
SD	26.6	32.5
N	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	116	99
8156	152	151
8160	151	117
8144	109	105

MEAN	132	118
SD	22.7	23.2
N	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: Heart RateSTUDY ID: 134  
STUDY NO: 134  
ABBR: HR

SEX: FEMALE

UNITS: bpm

ANIMAL ID      Pretest      Week 4

GROUP: 1-F:0 mg base/kg/day

8211	142	109
8214	102	83
8184	148	97
8180	106	101

MEAN	125	98
SD	23.9	10.9
N	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	119	70
8206	152	114
8185	84	127
8199	111	92

MEAN	117	101
SD	28.0	25.1
N	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	138	89
8193	156	103
8181	98	123
8197	150	130

MEAN	136	111
SD	26.1	18.7
N	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	67	72
8213	104	64
8194	123	93
8182	65	131

MEAN	90	90
SD	28.5	29.9
N	4	4

LABCAT CC4.25

DRAFT

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: P Wave DurationSTUDY ID: 134  
STUDY NO: 134  
ABBR: P

SEX: MALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-M:0 mg base/kg/day

8172	38	42
8143	41	41
8148	41	40
8153	41	46

MEAN	40	42
SD	1.5	2.6
N	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	45	43
8170	35	34
8147	38	45
8151	44	38

MEAN	41	40
SD	4.8	5.0
N	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	43	38
8159	38	40
8175	44	37
8166	35	38

MEAN	40	38
SD	4.2	1.3
N	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	38	41
8156	40	41
8160	41	40
8144	40	41

MEAN	40	41
SD	1.3	0.5
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: P Wave Duration

STUDY ID: 134  
STUDY NO: 134  
ABBR: P

SEX: FEMALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-F:0 mg base/kg/day

8211	36	43
8214	42	41
8184	39	42
8180	42	36

MEAN	40	41
SD	2.9	3.1
N	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	38	41
8206	38	37
8185	48	48
8199	41	42

MEAN	41	42
SD	4.7	4.5
N	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	41	39
8193	39	45
8181	44	47
8197	41	40

MEAN	41	43
SD	2.1	3.9
N	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	46	46
8213	40	37
8194	49	46
8182	29	35

MEAN	41	41
SD	8.8	5.8
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: PR Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: PR

SEX: MALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-M:0 mg base/kg/day

8172	96	93
8143	104	93
8148	101	97
8153	97	98

MEAN	100	95
SD	3.7	2.6
N	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	123	115
8170	98	96
8147	113	117
8151	103	104

MEAN	109	108
SD	11.1	9.8
N	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	89	79
8159	98	92
8175	100	84
8166	96	84

MEAN	96	85
SD	4.8	5.4
N	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	107	105
8156	97	93
8160	83	92
8144	89	79

MEAN	94	92
SD	10.4	10.6
N	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: PR IntervalSTUDY ID: 134  
STUDY NO: 134  
ABBR: PR

SEX: FEMALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-F:0 mg base/kg/day

8211	89	92
8214	95	86
8184	102	93
8180	102	97

MEAN	97	92
SD	6.3	4.5
N	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	90	86
8206	103	103
8185	117	95
8199	99	91

MEAN	102	94
SD	11.2	7.2
N	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	109	114
8193	100	113
8181	126	119
8197	104	94

MEAN	110	110
SD	11.4	11.0
N	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	110	98
8213	97	95
8194	101	98
8182	93	89

MEAN	100	95
SD	7.3	4.2
N	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: QRS IntervalSTUDY ID: 134  
STUDY NO: 134  
ABBR: QRS

SEX: MALE

UNITS: ms

ANIMAL ID	Pretest	Week 4
GROUP: 1-M:0 mg base/kg/day		
8172	40	42
8143	38	40
8148	37	38
8153	42	41
MEAN	39	40
SD	2.2	1.7
N	4	4

GROUP: 2-M:0.1 mg base/kg/day		
8173	42	44
8170	38	39
8147	40	41
8151	46	40
MEAN	42	41
SD	3.4	2.2
N	4	4

GROUP: 3-M:0.3 mg base/kg/day		
8157	41	42
8159	36	38
8175	37	40
8166	40	40
MEAN	39	40
SD	2.4	1.6
N	4	4

GROUP: 4-M:1.0 mg base/kg/day		
8146	39	40
8156	37	36
8160	38	38
8144	38	38
MEAN	38	38
SD	0.8	1.6
N	4	4

LABCAT CC4.25

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: QRS Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QRS

SEX: FEMALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-F:0 mg base/kg/day

8211	37	40
8214	38	40
8184	39	44
8180	33	46

MEAN	37	43
SD	2.6	3.0
N	4	4

GROUP: 2-F:0.1 mg base/kg/day

8207	38	38
8206	39	39
8185	39	39
8199	45	42

MEAN	40	40
SD	3.2	1.7
N	4	4

GROUP: 3-F:0.3 mg base/kg/day

8215	39	43
8193	39	39
8181	40	46
8197	37	47

MEAN	39	44
SD	1.3	3.6
N	4	4

GROUP: 4-F:1.0 mg base/kg/day

8196	36	37
8213	35	38
8194	41	41
8182	37	37

MEAN	37	38
SD	2.6	1.9
N	4	4

LABCAT CC4.25

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGSINDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: QT IntervalSTUDY ID: 134  
STUDY NO: 134  
ABBR: QT

SEX: MALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-M:0 mg base/kg/day

8172	220	210
8143	210	198
8148	174	174
8153	172	206

MEAN	194	197
SD	24.6	16.1
N	4	4

GROUP: 2-M:0.1 mg base/kg/day

8173	203	185
8170	176	169
8147	188	198
8151	189	189

MEAN	189	185
SD	11.0	12.1
N	4	4

GROUP: 3-M:0.3 mg base/kg/day

8157	194	182
8159	225	207
8175	218	210
8166	213	198

MEAN	213	199
SD	13.3	12.6
N	4	4

GROUP: 4-M:1.0 mg base/kg/day

8146	172	177
8156	187	166
8160	172	205
8144	184	191

MEAN	179	185
SD	7.9	16.9
N	4	4

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL CARDIOLOGY REPORT BY GROUP  
TEST: QT Interval

STUDY ID: 134  
STUDY NO: 134  
ABBR: QT

SEX: FEMALE

UNITS: ms

ANIMAL ID    Pretest    Week 4

GROUP: 1-F:0 mg base/kg/day  
8211            199            182  
8214            223            194  
8184            181            212  
8180            150            187  
  
MEAN            188            194  
SD              30.8          13.1  
N                4               4

GROUP: 2-F:0.1 mg base/kg/day  
8207            227            218  
8206            167            195  
8185            199            181  
8199            192            181  
  
MEAN            196            194  
SD              24.7          17.5  
N                4               4

GROUP: 3-F:0.3 mg base/kg/day  
8215            195            198  
8193            196            189  
8181            223            169  
8197            203            170  
  
MEAN            204            182  
SD              13.0          14.3  
N                4               4

GROUP: 4-F:1.0 mg base/kg/day  
8196            213            201  
8213            210            199  
8194            200            208  
8182            228            193  
  
MEAN            213            200  
SD              11.6          6.2  
N                4               4

LABCAT CC4.25

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APPENDIX 10  
Ophthalmology Report

# ANIMAL EYE ASSOCIATES

# DRAFT

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June 21, 1994

## OPHTHALMIC REPORT

UIC/TRL Study No. 134

### FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

On April 19, 1994, (Week -3), a sufficient number of male and female Beagle dogs were given ophthalmic examinations by indirect ophthalmoscopy to result in 16 dogs/sex which were within normal limits.

On May 31, 1994 (Week 4), the thirty-two Beagle dogs which were used in Study No. 134 were re-examined. All dogs appeared similar (no lesions) to their pretest examination on April 19, 1994.

Sincerely,



Samuel J. Vainisi, D.V.M.  
Professor of Comparative  
Ophthalmology, U. of IL. at Chicago

Diplomate, American College of  
Veterinary Ophthalmologists

## FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

## Ophthalmic Examinations

## Males

Dose	Animal Number	Week -3		Week 4	
		R.E.	L.E.	R.E.	L.E.
0	8172	WNL	WNL	WNL	WNL
	8148	WNL	WNL	WNL	WNL
	8148	WNL	WNL	WNL	WNL
	8153	WNL	WNL	WNL	WNL
0.1	8173	WNL	WNL	WNL	WNL
	8170	WNL	WNL	WNL	WNL
	8147	WNL	WNL	WNL	WNL
	8159	WNL	WNL	WNL	WNL
0.3	8157	WNL	WNL	WNL	WNL
	8159	WNL	WNL	WNL	WNL
	8175	WNL	WNL	WNL	WNL
	8166	WNL	WNL	WNL	WNL
1.0	8170	WNL	WNL	WNL	WNL
	8156	WNL	WNL	WNL	WNL
	8160	WNL	WNL	WNL	WNL
	8144	WNL	WNL	WNL	WNL

Dose = mg base/kg/day  
 R.E. = Right Eye  
 L.E. = Left Eye  
 WNL= Within Normal Limits

## FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

## Ophthalmic Examinations

## Females

Dose	Animal Number	Week -3		Week 4	
		R.E.	L.E.	R.E.	L.E.
0	8211	WNL	WNL	WNL	WNL
	8214	WNL	WNL	WNL	WNL
	8184	WNL	WNL	WNL	WNL
	8184	WNL	WNL	WNL	WNL
0.1	8207	WNL	WNL	WNL	WNL
	8206	WNL	WNL	WNL	WNL
	8193	WNL	WNL	WNL	WNL
	8199	WNL	WNL	WNL	WNL
0.3	8215	WNL	WNL	WNL	WNL
	8193	WNL	WNL	WNL	WNL
	8181	WNL	WNL	WNL	WNL
	8197	WNL	WNL	WNL	WNL
1.0	8196	WNL	WNL	WNL	WNL
	8213	WNL	WNL	WNL	WNL
	8194	WNL	WNL	WNL	WNL
	8182	WNL	WNL	WNL	WNL

Dose = mg base/kg/day  
 R.E. = Right Eye  
 L.E. = Left Eye  
 WNL= Within Normal Limits

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APPENDIX 11  
Individual Organ Weights

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day  
FATES: Scheduled Sacrifice DAYS: 28-29 ALL BALANCES

ANIMAL ID:	8143	8148	8153	8172
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	10.8	9.8	9.9	9.8
Adrenal Glands (G)	1.33	2.07	1.46	1.25
% BRAIN WEIGHT	1.90	2.74	1.82	1.50
Brain (G)	69.87	75.66	80.25	83.14
Heart (G)	84.79	82.29	75.06	87.40
% BRAIN WEIGHT	121.35	108.76	93.53	105.12
Kidneys (G)	50.90	46.03	44.04	44.68
% BRAIN WEIGHT	72.85	60.84	54.88	53.74
Liver (G)	251.43	259.15	238.30	268.52
% BRAIN WEIGHT	359.85	342.52	296.95	322.97
Spleen (G)	37.84	26.93	25.81	35.20
% BRAIN WEIGHT	54.16	35.59	32.16	42.34
Testes (G)	15.56	13.37	12.36	15.38
% BRAIN WEIGHT	22.27	17.67	15.40	18.50
Thyroid+Parathyroids (G)	0.98	0.98	0.69	0.96
% BRAIN WEIGHT	1.40	1.30	0.86	1.15

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: MALE

GROUP: 2-M - 0.1 mg base/kg/day  
FATES: Scheduled Sacrifice DAYS: 28-29 ALL BALANCES

ANIMAL ID:	8147	8151	8170	8173
BALANCE NO.:	2026	2026	2026	2027
BODY WEIGHT (KG)	9.4	9.1	10.3	11.1
Adrenal Glands (G)	1.14	1.29	1.33	1.24
% BRAIN WEIGHT	1.55	1.62	1.63	1.60
Brain (G)	73.76	79.59	81.45	77.37
Heart (G)	84.61	89.74	86.22	95.87
% BRAIN WEIGHT	114.71	112.75	105.86	123.91
Kidneys (G)	45.90	52.71	43.18	44.32
% BRAIN WEIGHT	62.23	66.23	53.01	57.28
Liver (G)	256.58	237.25	274.62	294.68
% BRAIN WEIGHT	347.86	298.09	337.16	380.87
Spleen (G)	26.81	24.54	34.74	36.50
% BRAIN WEIGHT	36.35	30.83	42.65	47.18
Testes (G)	15.70	12.66	10.13	10.96
% BRAIN WEIGHT	21.29	15.91	12.44	14.17
Thyroid+Parathyroids (G)	0.94	0.65	0.86	0.84
% BRAIN WEIGHT	1.27	0.82	1.06	1.09

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: MALE

GROUP: 3-M - 0.3 mg base/kg/day  
FATES: Scheduled Sacrifice DAYS: 28-29 ALL BALANCES

ANIMAL ID:	8157	8159	8166	8175
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	10.6	9.7	10.3	9.2
Adrenal Glands (G)	0.91	1.30	1.29	1.01
% BRAIN WEIGHT	1.08	1.80	1.46	1.39
Brain (G)	84.62	72.11	88.18	72.83
Heart (G)	81.88	77.82	85.60	74.50
% BRAIN WEIGHT	96.76	107.92	97.07	102.29
Kidneys (G)	42.37	46.83	49.45	46.79
% BRAIN WEIGHT	50.07	64.94	56.08	64.25
Liver (G)	260.58	277.14	267.74	284.09
% BRAIN WEIGHT	307.94	384.33	303.63	390.07
Spleen (G)	35.17	44.86	34.20	31.12
% BRAIN WEIGHT	41.56	62.21	38.78	42.73
Testes (G)	12.51	13.37	11.44	11.36
% BRAIN WEIGHT	14.78	18.54	12.97	15.60
Thyroid+Parathyroids (G)	1.03	1.48	0.96	1.52
% BRAIN WEIGHT	1.22	2.05	1.09	2.09

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: MALE

GROUP: 4-M - 1.0 mg base/kg/day  
FATES: Scheduled Sacrifice DAYS: 28-29 ALL BALANCES

ANIMAL ID:	8144	8146	8156	8160
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	8.8	9.2	9.6	10.4
Adrenal Glands (G)	1.14	1.20	1.12	1.13
% BRAIN WEIGHT	1.43	1.50	1.31	1.38
Brain (G)	79.75	79.96	85.21	81.62
Heart (G)	74.96	79.35	88.48	77.21
% BRAIN WEIGHT	93.99	99.24	103.84	94.60
Kidneys (G)	46.85	38.69	41.58	51.45
% BRAIN WEIGHT	58.75	48.39	48.80	63.04
Liver (G)	294.32	270.36	278.83	333.93
% BRAIN WEIGHT	369.05	338.12	327.23	409.13
Spleen (G)	64.92	59.09	50.29	63.58
% BRAIN WEIGHT	81.40	73.90	59.02	77.90
Testes (G)	12.21	13.03	12.74	14.08
% BRAIN WEIGHT	15.31	16.30	14.95	17.25
Thyroid+Parathyroids (G)	0.64	1.02	0.60	0.94
% BRAIN WEIGHT	0.80	1.28	0.70	1.15

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: FEMALE

GROUP: 1-F - 0 mg base/kg/day  
FATES: Scheduled Sacrifice DAYS: 28-29 ALL BALANCES

ANIMAL ID:	8180	8184	8211	8214
BALANCE NO.:	2026	2027	2026	2026
BODY WEIGHT (KG)	7.7	8.5	9.8	8.6
Adrenal Glands (G)	1.20	1.00	1.00	1.05
% BRAIN WEIGHT	1.65	1.48	1.42	1.41
Brain (G)	72.52	67.77	70.58	74.26
Heart (G)	76.38	76.87	69.67	82.90
% BRAIN WEIGHT	105.32	113.43	98.71	111.63
Kidneys (G)	33.75	42.18	36.68	36.32
% BRAIN WEIGHT	46.54	62.24	51.97	48.91
Liver (G)	188.47	299.94	233.04	233.03
% BRAIN WEIGHT	259.89	442.59	330.18	313.80
Ovaries (G)	0.63	0.98	0.77	0.79
% BRAIN WEIGHT	0.87	1.45	1.09	1.06
Spleen (G)	24.63	26.06	25.29	31.67
% BRAIN WEIGHT	33.96	38.45	35.83	42.65
Thyroid+Parathyroids (G)	0.67	0.94	0.78	0.66
% BRAIN WEIGHT	0.92	1.39	1.11	0.89

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

## INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: FEMALEGROUP: 2-F - 0.1 mg base/kg/day  
FATES: Scheduled Sacrifice      DAYS: 28-29      ALL BALANCES

ANIMAL ID:	8185	8199	8206	8207
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	8.9	9.3	9.1	8.6
Adrenal Glands (G)	1.27	1.23	1.37	1.55
% BRAIN WEIGHT	1.62	1.71	1.92	2.06
Brain (G)	78.50	71.80	71.22	75.22
Heart (G)	66.45	87.73	73.63	86.77
% BRAIN WEIGHT	84.65	122.19	103.38	115.35
Kidneys (G)	36.26	39.10	41.75	45.14
% BRAIN WEIGHT	46.19	54.46	58.62	60.01
Liver (G)	263.44	233.50	232.18	250.69
% BRAIN WEIGHT	335.59	325.21	326.00	333.28
Ovaries (G)	1.63	0.80	0.85	0.95
% BRAIN WEIGHT	2.08	1.11	1.19	1.26
Spleen (G)	26.80	35.54	32.30	25.54
% BRAIN WEIGHT	34.14	49.50	45.35	33.95
Thyroid+Parathyroids (G)	0.78	0.88	0.83	0.95
% BRAIN WEIGHT	0.99	1.23	1.17	1.26

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FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: FEMALE

GROUP: 3-F - 0.3 mg base/kg/day  
FATES: Scheduled Sacrifice      DAYS: 28-29      ALL BALANCES

ANIMAL ID:	8181	8193	8197	8215
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	8.5	9.0	8.1	9.5
Adrenal Glands (G)	1.23	1.47	1.05	1.29
% BRAIN WEIGHT	1.45	1.81	1.31	1.66
Brain (G)	84.77	81.39	79.87	77.73
Heart (G)	74.22	81.49	81.71	90.71
% BRAIN WEIGHT	87.55	100.12	102.30	116.70
Kidneys (G)	38.11	43.19	32.70	38.76
% BRAIN WEIGHT	44.96	53.07	40.94	49.86
Liver (G)	215.17	271.74	217.27	267.85
% BRAIN WEIGHT	253.83	333.87	272.03	344.59
Ovaries (G)	0.76	1.67	0.60	2.39
% BRAIN WEIGHT	0.90	2.05	0.75	3.07
Spleen (G)	32.29	34.79	33.57	47.66
% BRAIN WEIGHT	38.09	42.74	42.03	61.31
Thyroid+Parathyroids (G)	1.01	0.79	0.71	0.84
% BRAIN WEIGHT	1.19	0.97	0.89	1.08

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

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INDIVIDUAL ORGAN WEIGHTS

STUDY: 134  
SEX: FEMALE

GROUP: 4-F - 1.0 mg base/kg/day  
FATES: Scheduled Sacrifice      DAYS: 28-29      ALL BALANCES

ANIMAL ID:	8182	8194	8196	8213
BALANCE NO.:	2026	2026	2026	2026
BODY WEIGHT (KG)	7.7	8.8	9.2	8.0
Adrenal Glands (G)	1.16	1.34	1.40	1.12
% BRAIN WEIGHT	1.43	1.93	1.64	1.62
Brain (G)	81.10	69.45	85.29	69.12
Heart (G)	76.60	76.36	74.75	77.35
% BRAIN WEIGHT	94.45	109.95	87.64	111.91
Kidneys (G)	38.10	42.95	41.50	46.13
% BRAIN WEIGHT	46.98	61.84	48.66	66.74
Liver (G)	288.57	299.45	278.00	261.40
% BRAIN WEIGHT	355.82	431.17	325.95	378.18
Ovaries (G)	1.43	0.85	0.70	0.61
% BRAIN WEIGHT	1.76	1.22	0.82	0.88
Spleen (G)	52.18	60.23	119.73	66.35
% BRAIN WEIGHT	64.34	86.72	140.38	95.99
Thyroid+Parathyroids (G)	0.78	0.77	1.03	0.91
% BRAIN WEIGHT	0.96	1.11	1.21	1.32

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APPENDIX 12  
Pathology Report

Third Draft  
ANATOMIC PATHOLOGY REPORT FOR  
FOUR WEEK ORAL DOSE TOXICITY  
STUDY OF WR242511 IN DOGS

UIC/TRL STUDY NUMBER 134

September 12, 1994

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FOR  
TOXICOLOGY RESEARCH LABORATORY (M/C 868)  
DEPARTMENT OF PHARMACOLOGY  
UNIVERSITY OF ILLINOIS AT CHICAGO  
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SECTION I  
NARRATIVE

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## ANATOMIC PATHOLOGY REPORT

### FOUR WEEK ORAL DOSE TOXICITY STUDY OF WR242511 IN DOGS

#### INTRODUCTION

This report, submitted by Pathology Associates, Inc. (PAI) to Toxicology Research Laboratory (TRL), University of Illinois at Chicago, represents the histopathology findings for the study designated as "Four Week Oral Toxicity Study of WR242511 in Dogs", Toxicology Research Laboratory Study Number 134. The study was conducted at the University of Illinois at Chicago, Toxicology Research Laboratory where Barry S. Levine, D.Sc., D.A.B.T. served as the Study Director and Clyde W. Wheeler, Ph.D. was designated as the Study Toxicologist. Following in-life procedures, all dogs were humanely sacrificed and subjected to complete necropsy examination under the supervision of Michael J. Tomlinson, D.V.M., Ph.D., D.A.C.V.P. Collected tissue specimens, as required by the protocol, were processed into microslides at PAI's Chicago laboratory and forwarded to Richard H. Bruner, D.V.M., D.A.C.V.P. (PAI-Ohio) West Chester, Ohio for histopathological evaluation. All pathology procedures were conducted in accordance with FDA and EPA Good Laboratory Practice regulations, and a quality assurance statement has been included with this report.

#### EXPERIMENTAL DESIGN AND METHODS

Thirty-two Beagle dogs, 7-8 months old (16 males and 16 females) were divided into four treatment groups and dosed once daily (gelatin capsules) as outlined in the following experimental design:

##### Treatment Groups:

<u>Treatment Group</u>	<u>Dose Level (mg base/kg/day)</u>	<u>Number of Males</u>	<u>Number of Females</u>
1	0	4	4
2	0.1	4	4
3	0.3	4	4
4	1.0	4	4

Following treatment for four weeks, all animals were humanely sacrificed and necropsied in accordance with TRL Standard Operating Procedures. All protocol required tissues, as listed in Table I, were collected in 10% neutral buffered formalin, and subsequently processed into hematoxylin and eosin stained microslides according to PAI-Chicago Standard Operating Procedures. Prepared microslides were forwarded to the PAI-Ohio Division (West Chester) for histopathologic evaluations. Subsequently, all microscopic findings were entered into a validated pathology computer system (LABCAT), and the following reports were generated: 1) Project Summary tables listing the incidences of all neoplastic and non-neoplastic findings by treatment group (Section II); 2) Severity Summary tables listing group mean severity scores for all findings which received a severity grade\* (Section III); 3) Tabulated Animal Data tables outlining microscopic findings in individual animals by treatment group (Section IV); 4) Individual Animal Pathology records (Section V); and 5) Gross to Microscopic Correlations (Section VI). The codes used as entries in pathology tables are explained in the Reports Code Table (Table II) and Weighting Factors applied to severity scores are explained in the Severity Weighting Factors Table (Table III).

\* Where applicable histomorphologic changes were graded on a scale of 0 through 4, where 0 = no effect, 1 = minimal, 2 = mild, 3 = moderate and 4 = marked (severe). Group mean severity scores were determined by dividing the sum of all "weighted" severity scores for a particular histomorphologic change by the number of tissues examined. Weighting factors for individual severity grades were based upon the distribution of the lesion as explained in Table III.

#### EXPLANATIONS OF TREATMENT-RELATED MICROSCOPIC FINDINGS

**LUNGS:** Inflammation, interstitial (interstitial pneumonia) was characterized by patchy to confluent infiltrates of mixed inflammatory cells within alveolar lumina, septae and along the adventitial connective tissue of pulmonary blood vessels. Inflammatory cell populations included macrophages, small collections of neutrophils and occasional lymphocytes.

**SPLEEN:** Extramedullary hematopoiesis (EMH) was characterized by minimal to mild clusters of erythropoietic cells along with occasional megakaryocytes.

**BONE MARROW:** Hyperplasia was characterized by a diffuse increase in cells regarded as myeloid and erythroid precursors. In some specimens, erythroid cells appeared to be slightly more abundant than myeloid elements. Proliferating hematopoietic cells had largely replaced normal fat deposits in most of the marrow compartment.

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## RESULTS AND DISCUSSION

Although distinct treatment-related macroscopic (gross) changes were not observed, three animals given 1.0 mg base/kg/day (male #8144 and females #8182 and 8196) displayed white or yellow foci on the apical lobes of the lungs. These foci correlated with interstitial inflammation noted microscopically.

Microscopic changes considered to be treatment-related were observed in pulmonary, splenic and bone marrow sections of both males and females given 1.0 mg base/kg/day of the test material. Pulmonary changes consisting of diffuse, minimal to marked interstitial inflammation (Average Severity = 1.56) were noted in 3/4 (75%) males assigned to Group 4 (high dose). Similar findings were present in 4/4 (100%) high dose females; however, severity levels were slightly reduced, ranging from minimal to mild (Average Severity = 1.50). Splenic alterations, noted in 4/4 (100%) of both the high dose males and females, consisted of diffuse, minimal to mild extramedullary hematopoiesis (Average Severity = 1.50), where proliferating elements were largely of the erythroid cell series. Correspondingly, 4/4 (100%) of both the high dose males and females displayed diffuse, minimal to mild hyperplasia of bone marrow hematopoietic cells (Average Severity, males 0.75 and females 1.25). In bone marrow compartments, both erythroid and myeloid cells appeared to be increased when compared with control (Group 1) bone marrow sections. Microscopic changes observed in other animals assigned to this study were regarded as common, incidental findings with no relationship with the test material. Minimal to mild thymic involution was sporadically observed in several treatment groups, and 2/4 (50%) of the high dose females exhibited minimal thymic involution. In all affected dogs, thymic changes were regarded as a normal physiologic process or response to general body weight reduction rather than a target organ toxicity of the test material.

## CONCLUSIONS

Four week oral dosing resulted in minimal to marked pulmonary interstitial inflammation in 3/4 (75%) of the males and minimal to mild interstitial inflammation was noted in 4/4 (100%) of the females assigned to the high dose group (Group 4). Additionally, minimal to mild splenic extramedullary hematopoiesis and hyperplasia of bone marrow hematopoietic cells were present in all high dose animals. Distinct treatment-related histomorphologic changes were not observed in dogs assigned to other treatment groups. Based upon histomorphologic findings, 0.3 mg base/kg/day was selected as the no effect level under the conditions of this study.

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Richard H. Bruner, D.V.M.  
Diplomate, A.C.V.P.

---

Date

TABLE I

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## List of Tissues Examined Microscopically (TRL 134)

Adrenal glands	Nerve (sciatic)
Aorta	Ovaries
Brain (fore-, mid-, and hind-)	Pancreas
Cecum	Pituitary
Colon	Prostate
Diaphragm	Rectum
Duodenum	Rib with marrow
Epididymides	Salivary gland (submandibular)
Esophagus	Skin
Eyes and optic nerves	Spinal cord (thoracic, cervical)
Gallbladder	Spleen
Gross lesions	Stomach
Heart	Testes
Ileum	Thymus
Jejunum	Thyroid gland with parathyroids
Kidneys	Tongue
Liver (with gallbladder drained)	Tonsil
Lungs/bronchi	Trachea
Lymph node (submandibular)	Ureter
Lymph node (mesenteric)	Urinary bladder
Mammary gland	Uterus
Muscle (skeletal)	

TABLE II  
Reports Code Table

M	Multiple
N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable/unsuitable for evaluation
*	Tissues not examined/not required by protocol
()	Focal
<>	Multifocal
[]	Diffuse
1	Minimal
2	Mild
3	Moderate
4	Marked

TABLE III - SEVERITY WEIGHTING FACTORS

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The PAI pathology computer system (LABCAT) has a built-in weighting system for calculating the average severity for each tissue observation. These weighted averages are based upon the severity and distribution as outlined in the following table.

SEVERITY GRADING	NO MODIFIER	FOCAL	MULTIFOCAL	DIFFUSE
1	1.0	0.25	0.5	0.75
2	2.0	1.25	1.5	1.75
3	3.0	2.25	2.5	2.75
4	4.0	3.25	3.5	3.75

## EXAMPLE:

<u>TISSUE</u>	<u>DIAGNOSIS</u>	<u>SEVERITY</u>	<u>DISTRIBUTION</u>	<u>LABCAT SEVERITY SCORE</u>
Liver	Inflammation	Marked	None Entered	4.0
	Inflammation	Marked	Focal	3.25
	Inflammation	Marked	Multifocal	3.50
	Inflammation	Marked	Diffuse	3.75

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**SECTION II**  
**PROJECT SUMMARY TABLES**

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	#	%	#	%
FORE-BRAIN (CEREBRUM)	# EX 4	4	4	4
MID-BRAIN (MID-CEREBRUM)	# EX 4	4	4	4
HIND-BRAIN (CEREBELLUM)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, Chronic	2 50.0	0 0.0	1 25.0	1 25.0
Inflammation, Acute	1 25.0	0 0.0	0 0.0	0 0.0
ESOPHAGUS	# EX 4	4	4	4
LUNGS	# EX 4	4	4	4
Inflammation, Interstitial	0 0.0	0 0.0	0 0.0	3 75.0
Inflammation, Chronic	0 0.0	1 25.0	0 0.0	0 0.0
KIDNEY, RIGHT	# EX 4	4	4	4

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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PROJECT SUMMARY

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STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: MALE

---

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

---

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	#	%	#	%
KIDNEY, LEFT	# EX 4		4	
SPLEEN	# EX 4		4	
Extramedullary Hematopoiesis	0 0.0	1 25.0	0 0.0	4 100.0
PANCREAS	# EX 4		4	
DUODENUM	# EX 4		4	
LIVER	# EX 4		4	
Inflammation, Subacute	0 0.0	0 0.0	0 0.0	1 25.0
GALLBLADDER	# EX 4		4	
Inflammation, Chronic	1 25.0	0 0.0	1 25.0	1 25.0
ADRENAL GLAND	# EX 4		4	
SALIVARY GLAND	# EX 4		4	
MANDIBULAR LYMPH NODE	# EX 4		4	
Inflammation, Granulomatous	1 25.0	0 0.0	0 0.0	0 0.0
Eosinophilia	1 25.0	0 0.0	0 0.0	0 0.0
Pigmentation	1 25.0	0 0.0	0 0.0	0 0.0
Inflammation, Acute	2 50.0	1 25.0	0 0.0	0 0.0
JEJUNUM	# EX 3		4	

---

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	#	%	#	%
COLON	# EX 4	4	4	4
TONSIL	# EX 4	4	4	4
ILEUM	# EX 4	4	4	3
MESENTERIC LYMPH NODE	# EX 4	4	3	4
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	2
Involution	0 0.0	1 25.0	1 25.0	0 0.0
RECTUM	# EX 4	4	4	4
Hemorrhage, Acute	1 25.0	0 0.0	0 0.0	0 0.0
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 2	2	1	2
THYROID GLAND	# EX 4	4	4	4
C-Cell Hyperplasia	0 0.0	0 0.0	0 0.0	2 50.0

Incidence Calculated by No. of Tissues Scored  
(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# %	# %	# %	# %
PARATHYROID GLAND	# EX 4	3	3	2
Ultimobranchial Cyst	0 0.0	0 0.0	1 33.0	0 0.0
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 25.0	0 0.0	1 25.0	0 0.0
CECUM	# EX 4	4	4	4
STOMACH	# EX 4	4	4	4
URINARY BLADDER	# EX 4	4	4	4
Inflammation, Acute	0 0.0	0 0.0	0 0.0	1 25.0
TESTIS	# EX 4	4	4	4
Aspermatogenesis	0 0.0	1 25.0	0 0.0	0 0.0
EPIIDIOYMIS	# EX 4	4	4	4
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 3	4	2	4
EYE - RIGHT	# EX 4	4	4	4
OPTIC NERVE - RIGHT	# EX 3	4	4	4

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE

## INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# %	# %	# %	# %
EYE - LEFT	# EX 4	4	4	4
OPTIC NERVE - LEFT	# EX 4	4	4	4
RIB	# EX 4	4	4	4
BONE MARROW	# EX 4	4	4	4
Hyperplasia	0 0.0	0 0.0	0 0.0	4 100.0
PROSTATE	# EX 4	4	4	4
Immature	1 25.0	1 25.0	2 50.0	0 0.0

Incidence Calculated by No. of Tissues Scored  
(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# %	# %	# %	# %
FORE-BRAIN (CEREBRUM)	# EX 4	4	4	4
Hemorrhage, Acute	1 25.0	0 0.0	0 0.0	0 0.0
MID-BRAIN (MID-CEREBRUM)	# EX 4	4	4	4
HIND-BRAIN (CEREBELLUM)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
Hemorrhage, Acute	0 0.0	0 0.0	0 0.0	1 25.0
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, Chronic	2 50.0	1 25.0	1 25.0	0 0.0
ESOPHAGUS	# EX 4	4	4	4
LUNGS	# EX 4	4	4	4
Inflammation, Interstitial	0 0.0	0 0.0	0 0.0	4 100.0
Inflammation, Chronic	1 25.0	0 0.0	0 0.0	0 0.0
Alveolar Macrophages	0 0.0	0 0.0	1 25.0	0 0.0

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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PROJECT SUMMARY

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STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

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INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

---

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# %	# %	# %	# %
KIDNEY, RIGHT	# EX 4	4	4	4
KIDNEY, LEFT	# EX 4	4	4	4
SPLEEN	# EX 4	4	4	4
Extramedullary Hematopoiesis	0 0.0	0 0.0	0 0.0	4 100.0
PANCREAS	# EX 4	4	4	4
Lymphocytic Infiltrates	0 0.0	0 0.0	1 25.0	0 0.0
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Leukocytosis	0 0.0	0 0.0	0 0.0	1 25.0
GALLBLADDER	# EX 4	4	4	4
Inflammation, Chronic	0 0.0	0 0.0	0 0.0	1 25.0
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
MANDIBULAR LYMPH NODE	# EX 4	4	4	4
Inflammation, Acute	1 25.0	0 0.0	0 0.0	0 0.0
JEJUNUM	# EX 4	3	4	4

---

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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PROJECT SUMMARY

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STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

---

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

---

GROUP:		1	2	3	4
		(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:		4	4	4	4
		# %	# %	# %	# %
COLON	# EX	3	4	4	4
TONSIL	# EX	4	4	4	4
ILEUM	# EX	4	4	4	4
Hemorrhage		1 25.0	0 0.0	0 0.0	0 0.0
MESENTERIC LYMPH NODE	# EX	4	3	3	4
Hemorrhage		1 25.0	0 0.0	1 33.0	1 25.0
TONGUE	# EX	4	4	4	4
Inflammation, Chronic		1 25.0	0 0.0	0 0.0	0 0.0
DIAPHRAGM	# EX	4	4	4	4
THYMUS	# EX	4	4	4	4
Involution		0 0.0	1 25.0	0 0.0	2 50.0
RECTUM	# EX	4	4	4	4
SKELETAL MUSCLE	# EX	4	4	4	4
SKIN	# EX	4	4	4	4
Folliculitis		0 0.0	1 25.0	0 0.0	1 25.0
MAMMARY GLAND	# EX	1	3	3	1
Hypertrophy		0 0.0	1 33.0	1 33.0	1 100.0

---

Incidence Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# %	# %	# %	# %
MAMMARY GLAND	# EX 1	3	3	1
Hemorrhage	0 0.0	1 33.0	1 33.0	1 100.0
THYROID GLAND	# EX 4	4	4	4
PARATHYROID GLAND	# EX 3	4	3	4
Ultimobranchial Cyst	1 33.0	1 25.0	0 0.0	1 25.0
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 25.0	2 50.0	0 0.0	1 25.0
Inflammation, Acute	0 0.0	0 0.0	0 0.0	1 25.0
CECUM	# EX 4	4	4	4
STOMACH	# EX 4	4	4	4
URINARY BLADDER	# EX 4	4	4	4
OVARY	# EX 4	4	4	4
Cyst, Follicular	0 0.0	0 0.0	1 25.0	0 0.0
UTERUS	# EX 4	4	4	4
Hemorrhage	1 25.0	0 0.0	0 0.0	0 0.0
SCIATIC NERVE	# EX 4	4	4	4

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

PROJECT SUMMARY

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	#	%	#	%
URETER	# EX	4	4	4
Hemorrhage, Acute		0 0.0	0 0.0	2 50.0
EYE - RIGHT	# EX	4	4	4
OPTIC NERVE - RIGHT	# EX	4	4	4
EYE - LEFT	# EX	4	4	4
OPTIC NERVE - LEFT	# EX	4	3	3
RIB	# EX	4	4	4
BONE MARROW	# EX	4	4	4
Hyperplasia		0 0.0	0 0.0	4 100.0
Hyperplasia, Granulocytic		0 0.0	1 25.0	0 0.0
VAGINA	# EX	0	0	1
Cyst		0 0.0	0 0.0	1 100.0

Incidence Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

(END OF REPORT)

**SECTION III**  
**SEVERITY SUMMARY TABLES**

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY 10 : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
FORE-BRAIN (CEREBRUM)	# EX 4	4	4	4
MID-BRAIN (MID-CEREBRUM)	# EX 4	4	4	4
HIND-BRAIN (CEREBELLUM)	# EX 4	4	4	4
SPINAL CORD (CERVICAL)	# EX 4	4	4	4
SPINAL CORD (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, Chronic	2 0.19	0 0.00	1 0.19	1 0.06
Inflammation, Acute	1 0.19	0 0.00	0 0.00	0 0.00
ESOPHAGUS	# EX 4	4	4	4
LUNGS	# EX 4	4	4	4
Inflammation, Interstitial	0 0.00	0 0.00	0 0.00	3 1.56
Inflammation, Chronic	0 0.00	1 0.06	0 0.00	0 0.00
KIDNEY, RIGHT	# EX 4	4	4	4
KIDNEY, LEFT	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored  
(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY 10 : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
SPLEEN	# EX 4	4	4	4
Extramedullary Hematopoiesis	0 0.00	1 0.19	0 0.00	4 1.50
PANCREAS	# EX 4	4	4	4
DUODENUM	# EX 4	4	4	4
LIVER	# EX 4	4	4	4
Inflammation, Subacute	0 0.00	0 0.00	0 0.00	1 0.13
GALLBLADDER	# EX 4	4	4	4
Inflammation, Chronic	1 0.44	0 0.00	1 0.19	1 0.19
ADRENAL GLAND	# EX 4	4	4	4
SALIVARY GLAND	# EX 4	4	4	4
MANDIBULAR LYMPH NODE	# EX 4	4	4	4
Inflammation, Granulomatous	1 0.06	0 0.00	0 0.00	0 0.00
Eosinophilia	1 0.44	0 0.00	0 0.00	0 0.00
Pigmentation	1 0.13	0 0.00	0 0.00	0 0.00
Inflammation, Acute	2 0.38	1 0.31	0 0.00	0 0.00
JEJUNUM	# EX 3	4	4	4
COLON	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
TONSIL	# EX 4	4	4	4
ILEUM	# EX 4	4	4	3
MESENTERIC LYMPH NODE	# EX 4	4	3	4
TONGUE	# EX 4	4	4	4
DIAPHRAGM	# EX 4	4	4	4
THYMUS	# EX 4	4	4	2
Involution	0 0.00	1 0.44	1 0.44	0 0.00
RECTUM	# EX 4	4	4	4
Hemorrhage, Acute	1 0.06	0 0.00	0 0.00	0 0.00
SKELETAL MUSCLE	# EX 4	4	4	4
SKIN	# EX 4	4	4	4
MAMMARY GLAND	# EX 2	2	1	2
THYROID GLAND	# EX 4	4	4	4
C-Cell Hyperplasia	0 0.00	0 0.00	0 0.00	2 0.38
PARATHYROID GLAND	# EX 4	3	3	2
Ultimobranchial Cyst	0 0.00	0 0.00	1 0.08	0 0.00

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134

SEX: MALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 0.31	0 0.00	1 0.06	0 0.00
CECUM	# EX 4	4	4	4
STOMACH	# EX 4	4	4	4
URINARY BLADDER	# EX 4	4	4	4
Inflammation, Acute	0 0.00	0 0.00	0 0.00	1 0.19
TESTIS	# EX 4	4	4	4
Aspermatogenesis	0 0.00	1 0.06	0 0.00	0 0.00
EPIDIDYMIS	# EX 4	4	4	4
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 3	4	2	4
EYE - RIGHT	# EX 4	4	4	4
OPTIC NERVE - RIGHT	# EX 3	4	4	4
EYE - LEFT	# EX 4	4	4	4
OPTIC NERVE - LEFT	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored  
 (1) - 0 mg base/kg/day  
 (2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
 (4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
SEVERITY SUMMARY  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: MALE  
-----

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
-----				
	# SEV	# SEV	# SEV	# SEV
RIB	# EX 4	4	4	4
BONE MARROW	# EX 4	4	4	4
Hyperplasia	0 0.00	0 0.00	0 0.00	4 0.75
PROSTATE	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored  
(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY 10 : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
FORE-BRAIN (CEREBRUM)	# EX 4	4	4	4
Hemorrhage, Acute	1 0.06	0 0.00	0 0.00	0 0.00
MIO-BRAIN (MIO-CEREBRUM)	# EX 4	4	4	4
HINO-BRAIN (CEREBELLUM)	# EX 4	4	4	4
SPINAL CORO (CERVICAL)	# EX 4	4	4	4
Hemorrhage, Acute	0 0.00	0 0.00	0 0.00	1 0.13
SPINAL CORO (THORACIC)	# EX 4	4	4	4
HEART	# EX 4	4	4	4
AORTA	# EX 4	4	4	4
TRACHEA	# EX 4	4	4	4
Inflammation, Chronic	2 0.25	1 0.13	1 0.06	0 0.00
ESOPHAGUS	# EX 4	4	4	4
LUNGS	# EX 4	4	4	4
Inflammation, Interstitial	0 0.00	0 0.00	0 0.00	4 1.50
Inflammation, Chronic	1 0.13	0 0.00	0 0.00	0 0.00
Alveolar Macrophages	0 0.00	0 0.00	1 0.06	0 0.00
KIDNEY, RIGHT	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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SEVERITY SUMMARY

---

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

---

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4

---

	#	SEV	#	SEV	#	SEV	#	SEV
KIDNEY, LEFT	# EX	4		4		4		4
SPLEEN	# EX	4		4		4		4
Extramedullary Hematopoiesis		0 0.00		0 0.00		0 0.00		4 1.50
PANCREAS	# EX	4		4		4		4
Lymphocytic Infiltrates		0 0.00		0 0.00		1 0.13		0 0.00
DUODENUM	# EX	4		4		4		4
LIVER	# EX	4		4		4		4
Leukocytosis		0 0.00		0 0.00		0 0.00		1 0.19
GALLBLADDER	# EX	4		4		4		4
Inflammation, Chronic		0 0.00		0 0.00		0 0.00		1 0.44
ADRENAL GLAND	# EX	4		4		4		4
SALIVARY GLAND	# EX	4		4		4		4
MANDIBULAR LYMPH NODE	# EX	4		4		4		4
Inflammation, Acute		1 0.06		0 0.00		0 0.00		0 0.00
JEJUNUM	# EX	4		3		4		4
COLON	# EX	3		4		4		4

---

Severity Calculated by No. of Tissues Scored

(3) - 0.3 mg base/kg/day

(1) - 0 mg base/kg/day

(4) - 1.0 mg base/kg/day

(2) - 0.1 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

---

SEVERITY SUMMARY

---

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

---

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4

---

	#	SEV	#	SEV	#	SEV	#	SEV
TONSIL	# EX	4	4	4	4	4	4	4
ILEUM	# EX	4	4	4	4	4	4	4
Hemorrhage		1 0.19	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
MESENTERIC LYMPH NODE	# EX	4	3	3	4	4	4	4
Hemorrhage		1 0.19	0 0.00	1 0.08	1 0.19	1 0.19	1 0.19	1 0.19
TONGUE	# EX	4	4	4	4	4	4	4
Inflammation, Chronic		1 0.06	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00	0 0.00
DIAPHRAGM	# EX	4	4	4	4	4	4	4
THYMUS	# EX	4	4	4	4	4	4	4
Involution		0 0.00	1 0.19	0 0.00	2 0.38	2 0.38	2 0.38	2 0.38
RECTUM	# EX	4	4	4	4	4	4	4
SKELETAL MUSCLE	# EX	4	4	4	4	4	4	4
SKIN	# EX	4	4	4	4	4	4	4
Folliculitis		0 0.00	1 0.06	0 0.00	1 0.13	1 0.13	1 0.13	1 0.13
MAMMARY GLAND	# EX	1	3	3	1	1	1	1
Hypertrophy		0 0.00	1 0.25	1 0.25	1 1.75	1 1.75	1 1.75	1 1.75
Hemorrhage		0 0.00	1 0.17	1 0.17	1 1.75	1 1.75	1 1.75	1 1.75

---

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
THYROID GLAND	# EX 4	4	4	4
PARATHYROID GLAND	# EX 3	4	3	4
Ultimobranchial Cyst	1 0.08	1 0.06	0 0.00	1 0.06
PITUITARY GLAND	# EX 4	4	4	4
Cyst	1 0.06	2 0.38	0 0.00	1 0.31
Inflammation, Acute	0 0.00	0 0.00	0 0.00	1 0.19
CECUM	# EX 4	4	4	4
STOMACH	# EX 4	4	4	4
URINARY BLADDER	# EX 4	4	4	4
OVARY	# EX 4	4	4	4
Cyst, Follicular	0 0.00	0 0.00	1 0.38	0 0.00
UTERUS	# EX 4	4	4	4
Hemorrhage	1 0.44	0 0.00	0 0.00	0 0.00
SCIATIC NERVE	# EX 4	4	4	4
URETER	# EX 4	4	4	3
Hemorrhage, Acute	0 0.00	0 0.00	2 0.19	0 0.00
EYE - RIGHT	# EX 4	4	4	4

Severity Calculated by No. of Tissues Scored

(1) - 0 mg base/kg/day

(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day

(4) - 1.0 mg base/kg/day

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

## SEVERITY SUMMARY

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134

SEX: FEMALE

GROUP:	1	2	3	4
	(1)	(2)	(3)	(4)
NUMBER OF ANIMALS:	4	4	4	4
	# SEV	# SEV	# SEV	# SEV
OPTIC NERVE - RIGHT	# EX 4	4	4	4
EYE - LEFT	# EX 4	4	4	4
OPTIC NERVE - LEFT	# EX 4	4	3	3
RIB	# EX 4	4	4	4
BONE MARROW	# EX 4	4	4	4
Hyperplasia	0 0.00	0 0.00	0 0.00	4 1.25
Hyperplasia, Granulocytic	0 0.00	1 0.19	0 0.00	0 0.00
VAGINA	# EX 0	0	0	1

Severity Calculated by No. of Tissues Scored  
(1) - 0 mg base/kg/day  
(2) - 0.1 mg base/kg/day

(3) - 0.3 mg base/kg/day  
(4) - 1.0 mg base/kg/day

(END OF REPORT)

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**SECTION IV**  
**TABULATED ANIMAL DATA**

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8143	8148	8153	8172
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA			N	
Inflammation, Chronic	<1>	(1)	-	-
Inflammation, Acute	-	-	-	[1]
ESOPHAGUS	N	N	N	N
LUNGS	N	N	N	N
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

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TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 1: 0 mg base/kg/day  
 SEX: MALE

---

ANIMAL ID:	8143	8148	8153	8172
DUODENUM	N	N	N	N
LIVER	N	N	N	N
GALLBLADDER Inflammation, Chronic	-	-	-	[2]
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE		N		
Inflammation, Granulomatous	(1)	-	-	-
Eosinophilia	[2]	-	-	-
Pigmentation	<1>	-	-	-
Inflammation, Acute	-	-	[1]	[1]
JEJUNUM	N	N	U	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8143	8148	8153	8172
THYMUS	N	N	N	N
RECTUM		N	N	N
Hemorrhage, Acute	(1)	-	-	-
SKELETAL MUSCLE	N	N	N	N
SKIN	N	N	N	N
MAMMARY GLAND	N	U	U	N
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N	N	N
PITUITARY GLAND	N		N	N
Cyst	-	(2)	-	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N	N	N	N
EPIDIDYMIS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N	N	U	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: MALE

---

ANIMAL ID:	8143	8148	8153	8172
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	U	N	N
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N
PROSTATE	N		N	N
Immature	-	P	-	-

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8147	8151	8170	8173
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNGS	N		N	N
Inflammation, Chronic	-	(1)	-	-
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N		N
Extramedullary Hematopoiesis	-	-	[1]	-
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8147	8151	8170	8173
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE Inflammation, Acute	N	N	N	(2)
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS Involution	[2]	N	N	N
RECTUM	N	N	N	N
SKELETAL MUSCLE	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8147	8151	8170	8173
SKIN	N	N	N	N
MAMMARY GLAND	U	N	U	N
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N	U	N
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N	N		N
Aspermatogenesis	-	-	(1)	-
EPIDIDYMIS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N	N	N	N
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: MALE

---

ANIMAL ID:	8147	8151	8170	8173
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N
PROSTATE	N	N		N
Immature	-	-	P	-

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8157	8159	8166	8175
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N		N
Inflammation, Chronic	-	-	[1]	-
ESOPHAGUS	N	N	N	N
LUNGS	N	N	N	N
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8157	8159	8166	8175
LIVER	N	N	N	N
GALLBLADDER	N	N		N
Inflammation, Chronic	-	-	[1]	-
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N	U	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	
Involution	-	-	-	[2]
RECTUM	N	N	N	N
SKELETAL MUSCLE	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 3: 0.3 mg base/kg/day  
 SEX: MALE

---

ANIMAL ID:	8157	8159	8166	8175
SKIN	N	N	N	N
MAMMARY GLAND	N	U	U	U
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	U	N	N	
Ultimobranchial Cyst	-	-	-	(1)
PITUITARY GLAND		N	N	N
Cyst	(1)	-	-	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
TESTIS	N	N	N	N
EPIDIDYMIS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N	N	U	U
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: MALE

---

ANIMAL ID:	8157	8159	8166	8175
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N
PROSTATE		N	N	
Immature	P	-	-	P

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 4: 1.0 mg base/kg/day  
 SEX: MALE

---

ANIMAL ID:	8144	8146	8156	8160
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA Inflammation, Chronic	-	(1)	-	-
ESOPHAGUS	N	N	N	N
LUNGS Inflammation, Interstitial	[4]	[2]	-	[1]
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN Extramedullary Hematopoiesis	[2]	[1]	[2]	[2]
PANCREAS	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8144	8146	8156	8160
DUODENUM	N	N	N	N
LIVER	N		N	N
Inflammation, Subacute	-	<1>	-	-
GALLBLADDER	N	N	N	
Inflammation, Chronic	-	-	-	[1]
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	U	N	N
MESENTERIC LYMPH NODE	N	N	N	N
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	U	N	U
RECTUM	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day  
SEX: MALE

ANIMAL ID:	8144	8146	8156	8160
SKELETAL MUSCLE	N	N	N	N
SKIN	N	N	N	N
MAMMARY GLAND	N	U	N	U
THYROID GLAND	N			N
C-Cell Hyperplasia	-	[1]	[1]	-
PARATHYROID GLAND	U	U	N	N
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N		N	N
Inflammation, Acute	-	[1]	-	-
TESTIS	N	N	N	N
EPIDIDYMIS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N	N	N	N
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

GROUP: 4: 1.0 mg base/kg/day

SEX: MALE

---

ANIMAL ID:	8144	8146	8156	8160
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW Hyperplasia	[1]	[1]	[1]	[1]
PROSTATE	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8180	8184	8211	8214
FORE-BRAIN (CEREBRUM)	N	N	N	
Hemorrhage, Acute	-	-	-	(1)
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N			N
Inflammation, Chronic	-	[1]	(1)	-
ESOPHAGUS	N	N	N	N
LUNGS	N		N	N
Inflammation, Chronic	-	<1>	-	-
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8180	8184	8211	8214
DUODENUM	N	N	N	N
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N		N	N
Inflammation, Acute	-	(1)	-	-
JEJUNUM	N	N	N	N
COLON	U	N	N	N
TONSIL	N	N	N	N
ILEUM		N	N	N
Hemorrhage	[1]	-	-	-
MESENTERIC LYMPH NODE		N	N	N
Hemorrhage	[1]	-	-	-
TONGUE	N		N	N
Inflammation, Chronic	-	(1)	-	-
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
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-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity

FATE: ALL

STUDY NUMBER: 134

GROUP: 1: 0 mg base/kg/day

SEX: FEMALE  
-----

ANIMAL ID:	8180	8184	8211	8214
RECTUM	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
SKIN	N	N	N	N
MAMMARY GLAND	U	N	U	U
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N		N	U
Ultimobranchial Cyst	-	(1)	-	-
PITUITARY GLAND	N		N	N
Cyst	-	(1)	-	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARY	N	N	N	N
UTERUS	N		N	N
Hemorrhage	-	[2]	-	-
SCIATIC NERVE	N	N	N	N
URETER	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: FEMALE

---

ANIMAL ID:	8180	8184	8211	8214
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8185	8199	8206	8207
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA		N	N	N
Inflammation, Chronic	<1>	-	-	-
ESOPHAGUS	N	N	N	N
LUNGS	N	N	N	N
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N	N	N
PANCREAS	N	N	N	N
DUODENUM	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8185	8199	8206	8207
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N
JEJUNUM	N	U	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	U
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS		N	N	N
Involution	[1]	-	-	-
RECTUM	N	N	N	N
SKELETAL MUSCLE	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity

FATE: ALL

STUDY NUMBER: 134

GROUP: 2: 0.1 mg base/kg/day

SEX: FEMALE

---

ANIMAL ID:	8185	8199	8206	8207
SKIN	N	N	N	
Folliculitis	-	-	-	(1)
MAMMARY GLAND		N	N	U
Hypertrophy	[1]	-	-	-
Hemorrhage	<1>	-	-	-
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N		N
Ultimobranchial Cyst	-	-	(1)	-
PITUITARY GLAND		N		N
Cyst	(1)	-	(2)	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARY	N	N	N	N
UTERUS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N	N	N	N
EYE - RIGHT	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity

FATE: ALL

STUDY NUMBER: 134

GROUP: 2: 0.1 mg base/kg/day

SEX: FEMALE

---

ANIMAL ID:	8185	8199	8206	8207
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	N	N	N
RIB	N	N	N	N
BONE MARROW	N	N		N
Hyperplasia, Granulocytic	-	-	[1]	-

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 3: 0.3 mg base/kg/day  
 SEX: FEMALE

---

ANIMAL ID:	8181	8193	8197	8215
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N	N	N
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N		N
Inflammation, Chronic	-	-	(1)	-
ESOPHAGUS	N	N	N	N
LUNGS	N		N	N
Alveolar Macrophages	-	(1)	-	-
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN	N	N	N	N
PANCREAS	N	N	N	
Lymphocytic Infiltrates	-	-	-	<1>

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8181	8193	8197	8215
DUODENUM	N	N	N	N
LIVER	N	N	N	N
GALLBLADDER	N	N	N	N
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N		N	U
Hemorrhage	-	(1)	-	-
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS	N	N	N	N
RECTUM	N	N	N	N

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
 Study Number 134  
 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 3: 0.3 mg base/kg/day  
 SEX: FEMALE

---

ANIMAL ID:	8181	8193	8197	8215
SKELETAL MUSCLE	N	N	N	N
SKIN	N	N	N	N
MAMMARY GLAND	U	N	N	
Hypertrophy	-	-	-	[1]
Hemorrhage	-	-	-	<1>
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N	N	N	U
PITUITARY GLAND	N	N	N	N
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARY	N		N	N
Cyst, Follicular	-	<2>	-	-
UTERUS	N	N	N	N
SCIATIC NERVE	N	N	N	N
URETER	N			N
Hemorrhage, Acute	-	<1>	(1)	-
EYE - RIGHT	N	N	N	N

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See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
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of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: FEMALE

---

ANIMAL ID:	8181	8193	8197	8215
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	U	N	N
RIB	N	N	N	N
BONE MARROW	N	N	N	N

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
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 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity

FATE: ALL

STUDY NUMBER: 134

GROUP: 4: 1.D mg base/kg/day

SEX: FEMALE

---

ANIMAL ID:	8182	8194	8196	8213
FORE-BRAIN (CEREBRUM)	N	N	N	N
MID-BRAIN (MID-CEREBRUM)	N	N	N	N
HIND-BRAIN (CEREBELLUM)	N	N	N	N
SPINAL CORD (CERVICAL)	N	N		N
Hemorrhage, Acute	-	-	<1>	-
SPINAL CORD (THORACIC)	N	N	N	N
HEART	N	N	N	N
AORTA	N	N	N	N
TRACHEA	N	N	N	N
ESOPHAGUS	N	N	N	N
LUNGS				
Inflammation, Interstitial	[1]	[2]	[2]	[2]
KIDNEY, RIGHT	N	N	N	N
KIDNEY, LEFT	N	N	N	N
SPLEEN				
Extramedullary Hematopoiesis	[2]	[1]	[1]	[3]
PANCREAS	N	N	N	N

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

FATE: ALL

GROUP: 4: 1.0 mg base/kg/day

SEX: FEMALE  
-----

ANIMAL ID:	8182	8194	8196	8213
DUODENUM	N	N	N	N
LIVER	N	N	N	
Leukocytosis	-	-	-	[1]
GALLBLADDER		N	N	N
Inflammation, Chronic	[2]	-	-	-
ADRENAL GLAND	N	N	N	N
SALIVARY GLAND	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N
JEJUNUM	N	N	N	N
COLON	N	N	N	N
TONSIL	N	N	N	N
ILEUM	N	N	N	N
MESENTERIC LYMPH NODE	N		N	N
Hemorrhage	-	[1]	-	-
TONGUE	N	N	N	N
DIAPHRAGM	N	N	N	N
THYMUS		N	N	
Involution	[1]	-	-	[1]

-----  
See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
 Toxicology Research Laboratory  
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 Four Week Oral Toxicity Study  
 of WR242511 in Dogs

---

TABULATED ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
 FATE: ALL

STUDY NUMBER: 134  
 GROUP: 4: 1.0 mg base/kg/day  
 SEX: FEMALE

---

ANIMAL ID:	8182	8194	8196	8213
RECTUM	N	N	N	N
SKELETAL MUSCLE	N	N	N	N
SKIN	N		N	N
Folliculitis	-	<1>	-	-
MAMMARY GLAND		U	U	U
Hypertrophy	[2]	-	-	-
Hemorrhage	[2]	-	-	-
THYROID GLAND	N	N	N	N
PARATHYROID GLAND	N		N	N
Ultimobranchial Cyst	-	(1)	-	-
PITUITARY GLAND	N			N
Cyst	-	-	(2)	-
Inflammation, Acute	-	[1]	-	-
CECUM	N	N	N	N
STOMACH	N	N	N	N
URINARY BLADDER	N	N	N	N
OVARY	N	N	N	N
UTERUS	N	N	N	N
SCIATIC NERVE	N	N	N	N

---

See Reports Code Table for Symbol Definitions

Pathology Associates, Inc.  
Toxicology Research Laboratory  
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-----  
TABULATED ANIMAL DATA  
-----

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day  
SEX: FEMALE

ANIMAL ID:	8182	8194	8196	8213
URETER	N	N	N	U
EYE - RIGHT	N	N	N	N
OPTIC NERVE - RIGHT	N	N	N	N
EYE - LEFT	N	N	N	N
OPTIC NERVE - LEFT	N	U	N	N
RIB	N	N	N	N
BONE MARROW Hyperplasia	[2]	[2]	[1]	[1]
VAGINA Cyst	P	-	-	-

-----  
See Reports Code Table for Symbol Definitions

(END OF REPORT)

**SECTION V**  
**INDIVIDUAL ANIMAL PATHOLOGY RECORDS**

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8143  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, multifocal  
MANDIBULAR LYMPH NODE: Inflammation, Granulomatous, minimal, focal  
Eosinophilia, mild, diffuse  
Pigmentation, minimal, multifocal  
RECTUM: Hemorrhage, Acute, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; JEJUNUM; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; SKELETAL MUSCLE; SKIN; MAMMARY GLAND;  
THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS;  
EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT;  
RIB; BONE MARROW; PROSTATE

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Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

SEX: MALE

GROUP: 1: 0 mg base/kg/day

---

Animal ID: 8148

Pathologist: RHB

Animal Fate: Terminal Sacrifice

---

Reference to Necropsy Record:

Related Histopathology:

PROSTATE - Small

PROSTATE - Immature

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## MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, focal

PITUITARY GLAND: Cyst, mild, focal

PROSTATE: #Immature, Present

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## TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; THYROID GLAND; PARATHYROID GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS;  
SCIATIC NERVE; URETER; EYE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

## TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; OPTIC NERVE - RIGHT

---

# - Histologic change related to necropsy record data

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8153  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

MANDIBULAR LYMPH NODE: Inflammation, Acute, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID  
GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS;  
SCIATIC NERVE; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW;  
PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

JEJUNUM; MAMMARY GLAND; URETER

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Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8172  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Acute, minimal, diffuse  
GALLBLADDER: Inflammation, Chronic, mild, diffuse  
MANDIBULAR LYMPH NODE: Inflammation, Acute, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; ADRENAL GLAND; SALIVARY GLAND; JEJUNUM; COLON; TONSIL; ILEUM;  
MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; MAMMARY GLAND;  
THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS;  
EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT;  
RIB; BONE MARROW; PROSTATE

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Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA  
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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

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Animal ID: 8147  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

THYMUS: Involution, mild, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE;  
SKIN; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS;  
EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT;  
RIB; BONE MARROW; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND

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DRAFT

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Pathology Associates, Inc.  
Toxicology Research Laboratory  
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Four Week Oral Toxicity Study  
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INDIVIDUAL ANIMAL DATA

STUDY ID : 4 Week Oral Toxicity

STUDY NUMBER: 134

SEX: MALE

GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8151

Pathologist: RHB

Animal Fate: Terminal Sacrifice

MICROSCOPIC OBSERVATIONS:

LUNGS: Inflammation, Chronic, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; MAMMARY GLAND; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH;  
URINARY BLADDER; TESTIS; EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE -  
LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW; PROSTATE

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8170  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small

Related Histopathology:  
PROSTATE - Immature

MICROSCOPIC OBSERVATIONS:

SPLEEN: Extramedullary Hematopoiesis, minimal, diffuse  
TESTIS: Aspermatogenesis, minimal, focal  
PROSTATE: #Immature, Present

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; THYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; EPIDIDYMIS; SCIATIC  
NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; PARATHYROID GLAND

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8173  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

MANDIBULAR LYMPH NODE: Inflammation, Acute, mild, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; JEJUNUM; COLON;  
TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN;  
MAMMARY GLAND; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER;  
TESTIS; EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE  
- LEFT; RIB; BONE MARROW; PROSTATE

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8157  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small

Related Histopathology:  
PROSTATE - Immature

MICROSCOPIC OBSERVATIONS:

PITUITARY GLAND: Cyst, minimal, focal  
PROSTATE: #Immature, Present

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; MAMMARY GLAND; THYROID GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS;  
SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE  
MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:  
PARATHYROID GLAND

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8159  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID  
GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS;  
SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE  
MARROW; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MESENTERIC LYMPH NODE; MAMMARY GLAND

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Pathology Associates, Inc.  
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INDIVIDUAL ANIMAL DATA

STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8166  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, diffuse  
GALLBLADDER: Inflammation, Chronic, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON;  
TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN;  
THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS;  
EPIDIDYMIS; SCIATIC NERVE; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB;  
BONE MARROW; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; URETER

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8175  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small, 20x20mm

Related Histopathology:  
PROSTATE - Immature

MICROSCOPIC OBSERVATIONS:

THYMUS: Involution, mild, diffuse  
PARATHYROID GLAND: Ultimobranchial Cyst, minimal, focal  
PROSTATE: #Immature, Present

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE;  
SKIN; THYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS; SCIATIC  
NERVE; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; URETER

Pathology Associates, Inc.  
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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8144  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
LUNGS - Apical Lobe, Foci, Multiple, White

Related Histopathology:  
LUNGS - Inflammation, Interstitial

MICROSCOPIC OBSERVATIONS:

LUNGS: #Inflammation, Interstitial, marked, diffuse  
SPLEEN: Extramedullary Hematopoiesis, mild, diffuse  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS;  
DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON;  
TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN;  
MAMMARY GLAND; THYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS;  
SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

PARATHYROID GLAND

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8146  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, focal  
LUNGS: Inflammation, Interstitial, mild, diffuse  
SPLEEN: Extramedullary Hematopoiesis, minimal, diffuse  
LIVER: Inflammation, Subacute, minimal, multifocal  
THYROID GLAND: C-Cell Hyperplasia, minimal, diffuse  
URINARY BLADDER: Inflammation, Acute, minimal, diffuse  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS; DUODENUM;  
GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL;  
MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE; SKIN; PITUITARY GLAND; CECUM;  
STOMACH; TESTIS; EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT;  
OPTIC NERVE - LEFT; RIB; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

ILEUM; THYMUS; MAMMARY GLAND; PARATHYROID GLAND

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Pathology Associates, Inc.  
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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8156  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

SPLEEN: Extramedullary Hematopoiesis, mild, diffuse  
THYROID GLAND: C-Cell Hyperplasia, minimal, diffuse  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; MAMMARY GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER;  
TESTIS; EPIDIDYMIS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE  
- LEFT; RIB; PROSTATE

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: MALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8160  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

LUNGS: Inflammation, Interstitial, minimal, diffuse  
SPLEEN: Extramedullary Hematopoiesis, mild, diffuse  
GALLBLADDER: Inflammation, Chronic, minimal, diffuse  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS;  
DUODENUM; LIVER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND;  
PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; TESTIS; EPIDIDYMIS; SCIATIC  
NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; PROSTATE

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

THYMUS; MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8180  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

ILEUM: Hemorrhage, minimal, diffuse  
MESENTERIC LYMPH NODE: Hemorrhage, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; TONSIL; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND;  
PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE;  
URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

COLON; MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8184  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, diffuse  
LUNGS: Inflammation, Chronic, minimal, multifocal  
MANDIBULAR LYMPH NODE: Inflammation, Acute, minimal, focal  
TONGUE: Inflammation, Chronic, minimal, focal  
PARATHYROID GLAND: Ultimobranial Cyst, minimal, focal  
PITUITARY GLAND: Cyst, minimal, focal  
UTERUS: Hemorrhage, mild, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN; PANCREAS;  
DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; JEJUNUM; COLON; TONSIL; ILEUM;  
MESENTERIC LYMPH NODE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; MAMMARY GLAND; THYROID  
GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE -  
RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8211  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER;  
OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE -  
LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day

Animal ID: 8214  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

FORE-BRAIN (CEREBRUM): Hemorrhage, Acute, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL); SPINAL CORD (THORACIC);  
HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN; PANCREAS; DUODENUM;  
LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID  
GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE; URETER; EYE  
- RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; PARATHYROID GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8185  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, multifocal  
THYMUS: Involution, minimal, diffuse  
MAMMARY GLAND: Hypertrophy, minimal, diffuse  
Hemorrhage, minimal, multifocal  
PITUITARY GLAND: Cyst, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE;  
SKIN; THYROID GLAND; PARATHYROID GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC  
NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8199  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE;  
SKIN; MAMMARY GLAND; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY  
BLADDER; OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC  
NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

JEJUNUM

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8206  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

PARATHYROID GLAND: Ultimobranchial Cyst, minimal, focal  
PITUITARY GLAND: Cyst, mild, focal  
BONE MARROW: Hyperplasia, Granulocytic, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; MAMMARY GLAND; THYROID GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS;  
SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB

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INDIVIDUAL ANIMAL DATA

STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day

Animal ID: 8207  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

SKIN: Folliculitis, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; THYROID GLAND;  
PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE;  
URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MESENTERIC LYMPH NODE; MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8181  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER;  
OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE -  
LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8193  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

LUNGS: Alveolar Macrophages, minimal, focal  
MESENTERIC LYMPH NODE: Hemorrhage, minimal, focal  
OVARY: Cyst, Follicular, mild, multifocal  
URETER: Hemorrhage, Acute, minimal, multifocal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; MAMMARY  
GLAND; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; UTERUS;  
SCIATIC NERVE; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

OPTIC NERVE - LEFT

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Toxicology Research Laboratory  
Study Number 134  
Four Week Oral Toxicity Study  
of WR242511 in Dogs

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8197  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

TRACHEA: Inflammation, Chronic, minimal, focal  
URETER: Hemorrhage, Acute, minimal, focal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT; SPLEEN;  
PANCREAS; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE;  
JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL  
MUSCLE; SKIN; MAMMARY GLAND; THYROID GLAND; PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH;  
URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC  
NERVE - LEFT; RIB; BONE MARROW

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---

INDIVIDUAL ANIMAL DATA

---

STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day

Animal ID: 8215  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

PANCREAS: Lymphocytic Infiltrates, minimal, multifocal  
MAMMARY GLAND: Hypertrophy, minimal, diffuse  
Hemorrhage, minimal, multifocal

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; LUNGS; KIDNEY, RIGHT; KIDNEY, LEFT;  
SPLEEN; DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM;  
COLON; TONSIL; ILEUM; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND;  
PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT;  
OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB; BONE MARROW

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MESENTERIC LYMPH NODE; PARATHYROID GLAND

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INDIVIDUAL ANIMAL DATA  
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STUDY 10 : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8182  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
LIVER - Lesion, Mottled

Related Histopathology:  
LIVER - No Corollary change detected

VAGINA - Mucosa, Cyst, (1), 10x10x10mm, Round, Clear,  
Firm

VAGINA - Cyst

LUNGS - Left Apical Lobe, (1), Focus, 10x5mm, Round,  
Yellow

LUNGS - Inflammation, Interstitial

MICROSCOPIC OBSERVATIONS:

LUNGS: #Inflammation, Interstitial, minimal, diffuse  
SPLEEN: Extramedullary Hematopoiesis, mild, diffuse  
GALLBLADDER: Inflammation, Chronic, mild, diffuse  
THYMUS: Involution, minimal, diffuse  
MAMMARY GLAND: Hypertrophy, mild, diffuse  
Hemorrhage, mild, diffuse  
BONE MARROW: Hyperplasia, mild, diffuse  
VAGINA: #Cyst, Present

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MIO-BRAIN (MIO-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS;  
DUODENUM; LIVER; ADRENAL GLAND; SALIVARY GLAND; MANOIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND;  
PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE;  
URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB

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# - Histologic change related to necropsy record data

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INDIVIDUAL ANIMAL DATA

STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8194  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

LUNGS: Inflammation, Interstitial, mild, diffuse  
SPLEEN: Extramedullary Hematopoiesis, minimal, diffuse  
MESENTERIC LYMPH NODE: Hemorrhage, minimal, diffuse  
SKIN: Folliculitis, minimal, multifocal  
PARATHYROID GLAND: Ultimobranchial Cyst, minimal, focal  
PITUITARY GLAND: Inflammation, Acute, minimal, diffuse  
BONE MARROW: Hyperplasia, mild, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS;  
DUODENUM; LIVER; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON;  
TONSIL; ILEUM; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; THYROID GLAND; CECUM; STOMACH;  
URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT;  
RIB

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; OPTIC NERVE - LEFT

Pathology Associates, Inc.  
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INDIVIDUAL ANIMAL DATA

STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8196  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:

Related Histopathology:

LUNGS - Left Apical Lobe, Focus, (1), 15x10mm, Round,  
White

LUNGS - Inflammation, Interstitial

MICROSCOPIC OBSERVATIONS:

SPINAL CORD (CERVICAL): Hemorrhage, Acute, minimal, multifocal  
LUNGS: #Inflammation, Interstitial, mild, diffuse  
SPLEEN: Extramedullary Hematopoiesis, minimal, diffuse  
PITUITARY GLAND: Cyst, mild, focal  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (THORACIC); HEART;  
AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS; DUODENUM; LIVER; GALLBLADDER;  
ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL; ILEUM; MESENTERIC  
LYMPH NODE; TONGUE; DIAPHRAGM; THYMUS; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND; PARATHYROID  
GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE; URETER; EYE - RIGHT; OPTIC  
NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND

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INDIVIDUAL ANIMAL DATA

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STUDY ID : 4 Week Oral Toxicity  
SEX: FEMALE

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day

Animal ID: 8213  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

MICROSCOPIC OBSERVATIONS:

LUNGS: Inflammation, Interstitial, mild, diffuse  
SPLEEN: Extramedullary Hematopoiesis, moderate, diffuse  
LIVER: Leukocytosis, minimal, diffuse  
THYMUS: Involution, minimal, diffuse  
BONE MARROW: Hyperplasia, minimal, diffuse

TISSUES WITHIN NORMAL HISTOLOGICAL LIMITS:

FORE-BRAIN (CEREBRUM); MID-BRAIN (MID-CEREBRUM); HIND-BRAIN (CEREBELLUM); SPINAL CORD (CERVICAL);  
SPINAL CORD (THORACIC); HEART; AORTA; TRACHEA; ESOPHAGUS; KIDNEY, RIGHT; KIDNEY, LEFT; PANCREAS;  
DUODENUM; GALLBLADDER; ADRENAL GLAND; SALIVARY GLAND; MANDIBULAR LYMPH NODE; JEJUNUM; COLON; TONSIL;  
ILEUM; MESENTERIC LYMPH NODE; TONGUE; DIAPHRAGM; RECTUM; SKELETAL MUSCLE; SKIN; THYROID GLAND;  
PARATHYROID GLAND; PITUITARY GLAND; CECUM; STOMACH; URINARY BLADDER; OVARY; UTERUS; SCIATIC NERVE;  
EYE - RIGHT; OPTIC NERVE - RIGHT; EYE - LEFT; OPTIC NERVE - LEFT; RIB

TISSUES UNAVAILABLE FOR COMPLETE EVALUATION:

MAMMARY GLAND; URETER

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(END OF REPORT)

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**SECTION VI**  
**GROSS TO MICROSCOPIC CORRELATIONS**

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Pathology Associates, Inc.  
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CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: MALE

Animal ID: 8148  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small

Related Histopathology:  
PROSTATE - Immature

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CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: MALE

Animal ID: 8170  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small

Related Histopathology:  
PROSTATE - Immature

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Pathology Associates, Inc.  
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CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: MALE

Animal ID: 8157  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small

Related Histopathology:  
PROSTATE - Immature

Animal ID: 8175  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
PROSTATE - Small, 20x20mm

Related Histopathology:  
PROSTATE - Immature

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Pathology Associates, Inc.  
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of WR242511 in Dogs

CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day  
SEX: MALE

Animal ID: 8144  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
LUNGS - Apical Lobe, Foci, Multiple, White

Related Histopathology:  
LUNGS - Inflammation, Interstitial

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CORRELATION OF GROSS & MICRO

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STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 1: 0 mg base/kg/day  
SEX: FEMALE

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No Gross Observations for any animal in this group

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CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 2: 0.1 mg base/kg/day  
SEX: FEMALE

No Gross Observations for any animal in this group

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CORRELATION OF GROSS & MICRO

STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 3: 0.3 mg base/kg/day  
SEX: FEMALE

No Gross Observations for any animal in this group

Pathology Associates, Inc.  
Toxicology Research Laboratory  
Study Number 134  
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of WR242511 in Dogs

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CORRELATION OF GROSS & MICRO

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STUDY ID : 4 Week Oral Toxicity  
FATE: ALL

STUDY NUMBER: 134  
GROUP: 4: 1.0 mg base/kg/day  
SEX: FEMALE

---

Animal ID: 8182  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:  
LIVER - Lesion, Mottled

Related Histopathology:  
LIVER - No Corollary change detected

VAGINA - Mucosa, Cyst, (1), 10x10x10mm, Round, Clear,  
Firm

VAGINA - Cyst

LUNGS - Left Apical Lobe, (1), Focus, 10x5mm, Round,  
Yellow

LUNGS - Inflammation, Interstitial

---

Animal ID: 8196  
Animal Fate: Terminal Sacrifice

Pathologist: RHB

Reference to Necropsy Record:

LUNGS - Left Apical Lobe, Focus, (1), 15x10mm, Round,  
White

Related Histopathology:

LUNGS - Inflammation, Interstitial

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(END OF REPORT)

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**SECTION VII**  
**QUALITY ASSURANCE STATEMENT**

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### QUALITY ASSURANCE STATEMENT

The portions of this histopathology project performed and reported by Pathology Associates, Inc. has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Food and Drug Administration and Environmental Protection Agency. The following table is a record of the inspections/ audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management and Study Director</u>
09-12-94	Draft Report	09-12-94
08-31-94	Draft Report	08-31-94
08-11-94	Draft Report	08-11-94
06-24-94	Microtomy	06-27-94



Willa Fox, MA  
Quality Assurance Unit  
PAI-Cin

9-12-94

Date

TRL Study: 134

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APPENDIX 13

Protocol and Protocol Amendments

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Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-7J  
UIC/TRL Study No.: 134

FOUR WEEK ORAL TOXICITY STUDY  
OF WR242511 IN DOGS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine the toxicity of WR242511 tartrate in dogs following four weeks of daily administration by gelatin capsule. The protocol for this study was approved by the UIC Animal Care Committee (Appendix 1).

2.0 SPONSOR:

- 2.1 Name: U.S. Army Medical Materiel  
Development Activity
- 2.2 Address: Fort Detrick  
Frederick, MD 21702-5009
- 2.3 Representative: George J. Schieferstein, Ph.D.

3.0 TESTING FACILITY:

- 3.1 Name: Toxicology Research Laboratory (TRL)
- 3.2 Address: University of Illinois at Chicago (UIC)  
Department of Pharmacology  
1940 W. Taylor St.  
Chicago, Illinois 60612-7353
- 3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

- 4.1 Proposed Initiation of Dosing: 05/05/94
- 4.2 Proposed Necropsy Dates: 06/02-03/94
- 4.3 Proposed Study Completion Date  
(Draft Study Report): 09/02/94

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Contract No.: DAMD17-92-C-2001  
Task Order No.: UIC-7J  
UIC/TRL Study No.: 134

5.0 TEST ARTICLES

- 5.1 Name or Code No: WR242511 Tartrate  
Bottle Number - BM05816.
- 5.2 TRL Chemical No: 1720614
- 5.3 Physical Description: Yellow powder
- 5.4 Stability and Handling of Test Article:
- 5.4.1 Temperature: -20 to -15°C.
- 5.4.2 Humidity: Ambient conditions at -20 to -15°C.
- 5.4.3 Light: Protect from light.
- 5.4.4 Special Requirements: None.
- 5.5 Special Handling Procedures: Standard safety precautions will be followed including gloves, eye protection, mask, and lab coats.
- 5.6 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor.

6.0 PERSONNEL:

Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Toxicologist	Clyde W. Wheeler, Ph.D.
Pathologist	Michael J. Tomlinson, D.V.M., Ph.D., D.A.C.V.P.
Pathology Support	Ralph M. Bunte, D.V.M., D.A.C.V.P.
Analytical Chemist	Adam Negrusz, Ph.D.
Clinical Veterinarian	Terry Hewett, D.V.M.
Veterinarian Support	Documented in raw data
Cardiologist	Robert Hamlin, D.V.M., Ph.D., D.A.V.C.P.
Ophthalmologist	Samuel J. Vainisi, D.V.M., D.A.V.C.O.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Documented in raw data
Chemistry Specialist	Thomas Tolhurst, B.S.
Clinical Pathology	Maria Lang, A.H.T., C.V.T.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

- 7.1 Species: Dog
- 7.2 Strain: Beagle
- 7.3 Number and Sex: 16 Males and 16 Females
- 7.4 Age of Animals: Approximately 7 - 8 months old at dosing initiation.
- 7.5 Weight of Animals: Approximately 10 - 12 kg (males) and approximately 8 - 10 kg (females) at dosing initiation.
- 7.6 Source of Animals: Marshall Farms, North Rose, NY.
- 7.7 Justification for Selection of Test System: The FDA requires the use of two animal species, one being a non-rodent, in preclinical toxicology studies. The dog is a standard and accepted non-rodent species for regulatory toxicology studies, and is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival each animal will be given a facility unique number. This number will appear as an ear tattoo and will also appear on a cage card visible on the front of each run. The cage card will additionally contain the study number, test article identification, treatment group number and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC- accredited facility in a temperature (65 - 84°F) and humidity (50 ± 20%) controlled room with a 12 hour light/12 hour dark cycle. Animals may be housed two per run within sex during the quarantine/pretest period, but will be housed singly prior to dosing initiation for the duration of the study. The run size, at least 15 feet<sup>2</sup>, is adequate to house dogs at the upper weight range as described in the *Guide for the Care and Use of Laboratory Animals*, DHHS (NIH) No. 86.23. All runs will be cleaned and fresh bedding replaced daily. The runs will be sanitized once every two weeks.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately three weeks. During that time, the animals will be observed daily for signs of illness and all unusual observations will be reported to the Study Director, Toxicologist, or Clinical Veterinarian. Body weights and physical examinations will be done upon the dogs' arrival at the animal facility. Additionally, each dog will be lightly sprayed upon arrival with PARA PYRETHRIN MIST for fleas, lice, and ticks. Within one week of arrival, hematology and clinical chemistry tests, and fecal examination for internal parasites will be performed. If parasites other than coccidia are found, the affected animal will be treated with a vermifuge approved by the Sponsor, and at least 10 days and a negative fecal examination will elapse before the animal is used on a study. Animals which demonstrate coccidia in their fecal samples will only be treated in a similar manner as above if they concurrently exhibit diarrhea. All dogs will have been vaccinated against

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canine distemper, infectious canine hepatitis, leptospirosis, parainfluenza, parvo, oral papilloma, and rabies by the animal supplier. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animal will be eliminated from the animal selection process. If a selected animal appears sickly prior to initiation of treatment, it will be replaced by a healthy animal prior to treatment under the direction of the Study Director or Toxicologist. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.

- 7.11 Food: PMI Certified Canine Diet No. 5007 (PMI Feeds Inc., St. Louis, MO), approximately 400 g, will be provided daily from arrival until termination. Exactly 400g will be provided when food consumption is measured. The food will be removed for an overnight fast ( $\approx$  16 - 20 hours) prior to blood collection or scheduled sacrifice.
- 7.12 Water: Tap water from an automatic watering system in which the room distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is untreated with additional chlorine or HCl.
- 7.13 There are no known contaminants in the feed or water which are expected to influence the study. The results of bi-monthly comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.
- 7.14 It is not known if the animals will experience pain or distress during the study. Analgesic or anesthetic agents will confound the ability to determine the toxic potential of the test article, and therefore will not be used. If an animal is in severe pain or distress, following consultation with the veterinary staff, it will be euthanized in accordance with standard operating procedures."

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

<u>Treatment Group</u>	<u>Dose Level (mg base/kg/dav)</u>	<u>Number of Males</u>	<u>Number of Females</u>
1	0	4	4
2	0.1	4	4
3	0.3	4	4
4	1.0	4	4

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WR242511 dose levels will be selected on the basis of a previously conducted four week oral dose range-finding in dogs (UIC/TRL Study No. 133), following consultation with the Sponsor. The number of animals, 4 sex/dose, is routinely used in regulatory studies, and also is the number of animals for this species indicated in the FDA 1992 draft document entitled "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food (Redbook II), Short-Term Toxicity Tests with Rodents and Non-Rodents". No such FDA document exists for the testing of drugs.

The number of animals/group/sex is necessary for adequate statistical analysis.

- 8.2 Frequency and Route of Administration of the Test Article: The test article will be administered once daily by gelatin capsule starting with Day 0 for at least four weeks. All animals will receive empty gelatin capsules for at least the last 3 days during Week -1 to acclimate them to the procedure. The quantity of the test article (mg base/kg) will be adjusted on the basis of each animal's most recent body weight. Control animals will receive empty gelatin capsules. The animals will be dosed up to and including the day prior to scheduled necropsy on Day 28 or 29.
- 8.3 Justification of Route: The oral route is the intended clinical route and is specified by the Sponsor.
- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: The animals will be randomized using a restricted randomization procedure, stratified by body weight, during the quarantine/pretest period. Baseline data including clinical pathology and ophthalmology data will be used to select appropriate animals for randomization.
- 8.5 Test Article Vehicle: Gelatin capsules (size 000; capacity 1.37 ml).
- 8.6 Test Article Dosage Form Preparation and Analyses: Not applicable.
- 8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:
- 8.7.1 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing. Additionally, all animals will be observed for morbidity/mortality in the afternoon and immediately prior to dosing in the morning.
- 8.7.2 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices at randomization (Week -1) and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at randomization in Week -1, weekly thereafter, and at termination (Day 28 or 29).

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- 8.7.4 Food Consumption: Food consumption for all animals will be measured over an approximate 24 hour period twice during the quarantine/pretest period, and weekly thereafter.
- 8.7.5 Ophthalmologic Examinations: All animals will be examined by indirect ophthalmoscopy prior to study initiation and during Week 4.
- 8.7.6 Electrocardiographic Examinations: Recordings from leads I and aV<sub>F</sub> will be collected with the animal in right lateral recumbency during the quarantine period and in Week 4. Analysis will include heart rate and duration of the P wave and PR, QRS and QT intervals.
- 8.7.7 Clinical Pathology: Hematology and clinical chemistry parameters will be measured following an overnight fast within one week of arrival in Week -3, Week -2/Week -1, after approximately one week of dosing and at termination in Week 5. In addition, methemoglobin levels will be measured weekly commencing on Day 0, just prior to dosing. The animals will be unanesthetized and sufficient blood will be collected from the jugular vein to measure the following parameters in random order.

## Hematology

Activated partial thromboplastin time	Mean corpuscular hemoglobin (MCH)
Erythrocyte count	Mean corpuscular hemoglobin concentration (MCHC)
Erythrocyte morphology	Mean corpuscular volume (MCV)
Heinz bodies	*Methemoglobin
Hematocrit	Platelet count
Hemoglobin	Prothrombin time
Leukocyte count, total and differential	Reticulocyte count

\* To be measured with a Co-oximeter (Instrumentation Laboratory, Model No. 282). The assay will be performed within one-hour of sample collection. The specimens will be kept on wet ice prior to analysis.

## Clinical Chemistry

Alanine aminotransferase (ALT/SGPT)	Globulin (calculated)
Albumin	Glucose
Albumin/globulin ratio (calculated)	Haptoglobin
Alkaline phosphatase	Lactate dehydrogenase (LDH)
Aspartate aminotransferase (AST/SGOT)	Phosphorus (inorganic)
Calcium	Potassium
Chloride	Sodium
Cholesterol	Total bilirubin
Creatinine	Total protein
Creatine kinase (CK)	Triglycerides
Gamma glutamyl transferase	Urea nitrogen (BUN)

Urinalysis parameters will be measured following an overnight fast at scheduled termination in Week 5. During the overnight fasting period, the animals will be placed in a metabolism cage for urine collection. Water will be available *ad libitum* during all fasting periods.

#### Urinalysis

Qualitative	
Bilirubin	Nitrite
Glucose	pH
Ketones	Protein
Occult blood	Urobilinogen
Leukocytes	
Color	
Specific Gravity	
Microscopic examination of spun sediment	

- 8.7.8 Plasma and Blood Cell Isolation: Just prior to dosing, a minimum of 2.5 ml of blood will be collected from the jugular vein weekly beginning on Day 0 for the separation and isolation of plasma and cellular blood components according to the Sponsor's directives. The plasma and cell fractions resulting from separation by centrifugation will be sent to Col. Thomas Brewer, MD as specified by the Sponsor. The results obtained from these samples will not be included in the study report.
- 8.7.9 Pathology: All animals which die on test or are killed if moribund will be necropsied. All remaining animals will be killed and necropsied in random order over a two consecutive day period (Days 28 and 29). This will be accomplished by sodium pentobarbital anesthesia (i.v.; 20-30 mg/kg) and exsanguination. An extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass to include the external surface, all orifices, the cranial cavity, external surface of the brain, cross section of the spinal cord, the nasal cavity and nasal turbinates, thoracic, abdominal and pelvic cavities and their viscera, and cervical tissues and organs. The following tissues and organs will be collected and fixed in 10% neutral buffered formalin (NBF).

REVISED PAGE	
STUDY NO: 134	INITIAL: <i>BM</i>
DATE: 12-9-93	

Contract No.: DAMD17-92-C-2001  
 Task Order No.: UIC-7J  
 UIC/TRL Study No.: 134

*Adrenal glands	Nerve (sciatic)
Aorta (thoracic)	*Ovaries
*Brain (fore-, mid-, and hind-)	Pancreas
Cecum	Pituitary
Colon	Prostate
Diaphragm	Rectum
Duodenum	Rib with marrow
Epididymides	Salivary gland (mandibular)
Esophagus	Skin
Eyes and optic nerve	Spinal cord (thoracic, cervical)
Gall bladder	*Spleen
Gross lesions	Stomach
*Heart	*Testes
Ileum	Thymus
Jejunum	*Thyroid gland with parathyroids
*Kidneys	Tongue
*Liver (with gall bladder drained)	Tonsil
Lungs/Bronchi	Trachea
Lymph node (submandibular)	Ureter
Lymph node (mesenteric)	Urinary bladder
Mammary gland	Uterus
Muscle (skeletal)	
* Weighed at scheduled necropsy	
Paired organs will be weighed as a unit.	

All tissues collected at necropsy from all dogs in all treatment groups found dead, sacrificed either *in extremis* or at scheduled necropsy in Week 5 will be embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined microscopically.

In addition to the collection of the aforementioned tissues and organs, five tubes of heparinized blood ( $\approx 250$  ml) will be routinely collected at euthanasia and bile will be aspirated by syringe from the gall bladder at necropsy according to the Sponsor's directives. The samples will be sent to Col. Thomas G. Brewer, MD as specified by the Sponsor, and the results obtained from these samples will not be included in the study report.

8.7.11 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, hematology, clinical chemistry and organ weight data. Organ weight analyses will consider weights relative to brain weight. If a significant F ratio is obtained ( $p \leq 0.05$ ), Dunnett's t test will be used for pairwise comparisons to the control group. Food consumption data will be analyzed by the Kruskal-Wallis test ( $p \leq 0.05$ ). If a significant effect is seen, the Mann-Whitney U test will be used for pairwise comparisons to the control group. Frequency data such as incidence of mortality, gross necropsy observations and tissue morphology observations will be compared by Fishers Exact Test or Chi-square analyses as necessary. Quantitative data will be tabulated and presented in the report. In

addition to the written report, summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette) in "ASCII" form. The transcribed data on disk will no longer be considered GLP compliant.

#### 9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct of the study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data.

Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct data input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) shall be made in such a manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified.

All recorded data shall be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives maintained by Quality Assurance.

All changes or revisions, and reasons therefore, to this protocol once it is approved shall be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

#### 10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards.

Will this study be submitted to a regulatory agency? Yes If so, to which agency(ies)? Food and Drug Administration

Does the Sponsor Request that test article samples be returned? Possibly; direction to be provided by the Sponsor.

Does the Sponsor request that samples of the test article/carrier mixture(s) be returned to the Sponsor? Not applicable

#### 11.0 PROTOCOL APPROVAL:

11.0 PROTOCOL APPROVAL:

DRAFT

STUDY DIRECTOR:

  
Barry S. Levine, D.Sc., D.A.B.T.

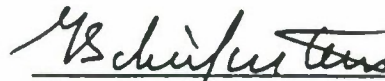
11/14/93  
Date

QUALITY ASSURANCE:

  
Ronald Schoenbeck

11/22/93  
Date

SPONSOR APPROVAL:

  
George J. Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

12/13/93.  
Date

COMMENTS FROM THE COR:

Office of the Vice Chancellor for Research (M/C 672)  
310 Administrative Office Building  
1737 West Polk Street  
Chicago, Illinois 60612-7227  
(312) 996-4995

Appendix 1

**DRAFT**

November 22, 1993

Barry S. Levine  
Med-Pharmacology  
312 BGRC, M/C 868

Dear Dr. Levine:

The protocol indicated below has been reviewed in accordance with the Animal Care Policies of the University of Illinois at Chicago and approved on May 18, 1993.

**Title of Application: Four Week Oral Toxicity Study of WR242511 In Dogs**

**ACC Number: 93-033-14**

This institution has Animal Welfare Assurance Number A3460.01 on file with the Office for Protection from Research Risks, NIH. Please transmit this letter of acceptable verification of your research protocol to your sponsor.

Thank you for complying with the Animal Care Policies and Procedures of UIC.

Sincerely yours,

*Josephine B. Miller*  
Josephine B. Miller, Ph.D.  
Chair, Animal Care Committee

JBm:st  
xc:BRL

PROTOCOL AMENDMENT

DRAFT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

1. Page 2 Section 5.1

Indicate the Bottle Number of the test article; "BM05816".

Reason: Sponsor requested that specific bottle number be included in the protocol.

2. Page 2 Section 6.0

Add "Cardiologist; Robert Hamlin, D.V.M., Ph.D., D.A.V.C.P." to the personnel list.

Reason: Sponsor requested ECG measurements be taken, necessitating the addition of Dr. Hamlin to interpret the findings.

3. Page 4 Section 7

Add the following section:

"7.14 It is not known if the animals will experience pain or distress during the study. Analgesic or anesthetic agents will confound the ability to determine the toxic potential of the test article, and therefore will not be used. If an animal is in severe pain or distress, following consultation with the veterinary staff, it will be euthanized in accordance with standard operating procedures."

Reason: Sponsor requested addition to the protocol.

4. Page 5 Section 8.1

Add the following sentences to the end of the first paragraph "The number of animals, 4 sex/dose, is routinely used in regulatory studies, and also is the number of animals for this species indicated in the FDA 1992 draft document entitled "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food (Redbook II), Short-Term Toxicity Tests with Rodents and Non-Rodents". No such FDA document exists for the testing of drugs.

Reason: Sponsor requested addition to the protocol.

5. Page 5 Section 8.5

Change the test article vehicle section to read the following "Gelatin capsules (size 000; capacity 1.37 ml)."

PROTOCOL AMENDMENT

DRAFT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

Reason: Clarification of the size and the capacity of the gelatin capsules to be used.

6. Page 5 Section 8.7

Insert the following section to the protocol before clinical pathology. This will subsequently cause the renumbering of sections following Section 8.7.6.

"8.7.6 Electrocardiographic Examinations: Recordings from leads I, II, III, aV<sub>F</sub>, aV<sub>L</sub> and aV<sub>R</sub> will be collected during the quarantine period and in Week 4. Analysis will include heart rate and duration of the P wave and PR, QRS and QT intervals."

Reason: Sponsor requested that ECG measurements be included in the study.

7. Page 5 Former Section 8.7.6.; currently Section 8.7.7 (see amendment 6)

Change the first sentence to indicate that clinical pathology parameters will be measured twice in the pre-test period, once within one week of arrival in Week -3 and in Week -1.

Reason: Mistake in the protocol.

8. Page 7 Section 8.7.8

Change first sentence to indicate that all blood collection will be done "just prior to dosing" and that the plasma and cellular components will be separated according to the Sponsor's directives.

Reason: Clarification of the time when blood collection will be performed and that the separation will be performed according to the SOP provided by the Sponsor.

9. Page 7 Section 8.7.9

Add "(i.v.; 20-30 mg/kg)" after "sodium pentobarbital anesthesia".

Reason: Clarification of the dose and route of pentobarbital.

10. Page 8 Section 8.7.9

Change second paragraph to indicate that "≈ 250 ml" of heparinized blood will be collected at euthanasia and bile at necropsy according to the Sponsor's directives in an SOP to be provided by the Sponsor.

PROTOCOL AMENDMENT

DRAFT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

Reason: Sponsor requested change in the protocol.

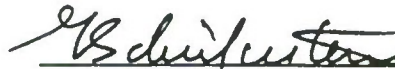
Approvals:

STUDY DIRECTOR:

  
Barry S. Levine, D.Sc. D.A.B.T.

12/10/93  
Date

SPONSOR APPROVAL:

  
George J. Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

12/13/93 .  
Date

PROTOCOL AMENDMENT

DRAFT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

11. Page 1 Section 4.0

Add the study dates as follows:

- |     |   |             |
|-----|---|-------------|
| 4.1 | <u>Proposed Initiation of Dosing:</u>                                 | 05/05/94    |
| 4.2 | <u>Proposed Necropsy Dates:</u>                                       | 06/02-03/94 |
| 4.3 | <u>Proposed Study Completion Date</u><br><u>(Draft Study Report):</u> | 09/02/94    |

Reason: The study dates have been finalized.

12. Page 3 Section 7.9

Change the paragraph to indicate that animals may be housed two per run in the quarantine/pre-test period, but that prior to initiation of dosing all animals will be housed singly.

Reason: Clarification of the protocol.

13. Page 3 Section 7.10

Change paragraph to indicate that healthy dogs which demonstrate coccidia in fecal samples will not be treated with medications unless they also exhibit clinical signs of diarrhea.

Reason: The presence of coccidia is considered incidental by the clinical veterinarian. Also, current medications do not eliminate the parasite from the canine host, but rather stop the shedding of the parasite.

14. Page 4 Section 7.11

Change the source of the canine diet from "Ralston Purina Company" to "PMI Feeds, Inc.".

Reason: Mistake in the protocol. The company has changed its name.

DRAFT

PROTOCOL AMENDMENT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

15. Page 4 Section 8.1

Change the dose levels as follows:

"Low" = "0.1" mg base/kg/day

"Mid" = "0.3" mg base/kg/day

"High" = "1.0" mg base/kg/day

Reason: Dose levels have been selected following consultation with the Sponsor.

16. Page 5 Section 8.2

Change second sentence to indicate that animals will be acclimated to the procedure of receiving gelatin capsules for "at least" the last 3 days during Week -1.

Reason: Clarification of the protocol.

17. Page 6 Section 8.7.6

Change the first sentence to indicate that recordings will only be collected from leads I and aV<sub>F</sub> with the animal in right lateral recumbency.

Reason: Clarification of the protocol at the request of the cardiologist.

18. Page 6 Section 8.7.7

In the first sentence change from "Week -1" to "Week -2/Week -1" regarding the time period when hematology and clinical pathology parameters will be measured.

Reason: Because of the number of animals and since both toxicity studies of the anti-cyanide drugs are being conducted concurrently (starting a few days apart), this required that clinical pathology parameters be measured in Week -2 for some animals.

DRAFT

PROTOCOL AMENDMENT

Study No.: 134

Title: Four Week Oral Toxicity Study of WR242511 in Dogs

19. Page 8 Section 8.7.10

Change first sentence in the second paragraph to indicate that five tubes of heparinized blood ( $\approx$  250 ml) will be "routinely" collected at euthanasia, etc..

Reason: Clarification of the protocol to allow for the possible inability to collect the desired amount of blood before the dog expires (heart stops beating) making further collection of blood not possible.


20. Page 8 Section 8.7.11

Indicate that organ weight analysis will consider weights relative to brain weights only. Analysis will not consider absolute weights or weights relative to body weight as previously indicated.

Reason: Sponsor requested change in the protocol.

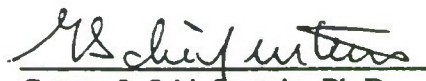
Approvals:

STUDY DIRECTOR:

  
Barry S. Levine, D.Sc., D.A.B.T.

5/1/94  
Date

SPONSOR APPROVAL:

  
George J. Schieferstein, Ph.D.  
Contracting Officer's  
Representative (COR)

5/19/94  
Date

DRAFT

APPENDIX 14  
Study Deviations

FOUR WEEK ORAL TOXICITY STUDY OF WR242511 IN DOGS

DRAFT

Study Deviations\*

<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	On one occasion during the pretest/study period, the relative humidity in the animal room deviated outside the specified range by +8%.	None. This occurrence was not considered to have had an impact on the outcome of the study.

\*The detailed "Deviation Report" is contained in the raw data which is archived at the University of Illinois at Chicago, Department of Pharmacology, Chicago, Illinois.

The above deviation did not affect the integrity of the study.

\_\_\_\_\_  
Barry S. Levine, D.Sc., D.A.B.T.

\_\_\_\_\_  
Date